# 2017

# YOUNG INVESTIGATOR

# GRANT PROGRAM

## ANNOUNCEMENT OF YOUNG INVESTIGATOR GRANTEES

BRAIN &
BEHAVIOR
RESEARCH FOUNDATION

Awarding **NARSAD** Grants

| 177 | 2 | 2 | 4 | 13 | 26 | 52 |
|---|---|---|---|---|---|---|
| Members | Nobel Prize Winners | Former Directors of the National Institute of Mental Health as well as the Current Director | Recipients of the National Medal of Science | Members of the National Academy of Sciences | Chairs of Psychiatry & Neuroscience Departments at Leading Medical Institutions | Members of the National Academy of Medicine |

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# Summary of 2017 Young Investigator Grants by Illness

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# About the Young Investigator Grant Program

Initiated in 1987, the Foundation's Young Investigator Grant provides support for the most promising young scientists conducting neurobiological research. This program is intended to facilitate innovative research opportunities and supports basic science, as well as translational and/or clinical investigators. All research must be relevant to our understanding, treatment and prevention of serious brain and behavior disorders such as schizophrenia, mood disorders, anxiety disorders or child and adolescent mental illnesses.

The Young Investigator Grant program helps launch neuroscience and psychiatry careers and expedites the gathering of crucial pilot data necessary for future funding.

## A UNIQUE GRANT PROGRAM

Research projects to be funded are selected by our world-renowned Scientific Council comprised of 177 leading researchers across disciplines in brain and behavior research. The Scientific Council was founded and is led by Dr. Herbert Pardes, a former director of the NIMH and the Executive Vice Chairman of the Board of Trustees at NewYork-Presbyterian Hospital. All of our grants are funded by private contributions and 100 percent of contributions for research go directly into our grants thanks to the generosity of two family foundations that cover operational expenses of the Foundation.

Only innovative, cutting-edge projects get funded.

Two-year awards up to $70,000 or $35,000 per year are provided to enable promising investigators to either extend research fellowship training or begin careers as independent research faculty.

The grants have proven to be catalytic—they have led to subsequent grant funding on average 11–19 times the original grant amount.

## Since 1987

**4,282**
Young Investigator
Grants Awarded

**$257M**
More than
$257 Million Funded

**$2.5B**
Resulting in more than
$2.5 Billion in Subsequent
Research Funding

## In 2017

**864**
Applications

**196**
Grants Awarded

**$13.6M**
Million Funded

# Co-Chairs of the Young Investigator Grant Selection Commitee

**Judy M. Ford, Ph.D.**

Professor, Department of Psychiatry
University of California, San Francisco

2003 Independent Investigator

Co-Chair of the Young Investigator Selection Committee
and Foundation Scientific Council Member

"These grants to young investigators are the mother's milk for launching a career in research. They come at a time when these young researchers are starting their own programs of research, and they need both the recognition and funding that these YI awards provide. The applicants, and their proposals this past year [2017], were outstanding. It was often difficult to choose the best of the best."

**Suzanne N. Haber, Ph.D.**

Professor, Department of Pharmacology and Physiology
University of Rochester School of Medicine and Dentistry

2011 Distinguished Investigator

Co-Chair of the Young Investigator Selection Committee
and Foundation Scientific Council Member

"This year we had an especially outstanding group of Young Investigator applicants. It's exciting to be able to help these young stars reach their goals."
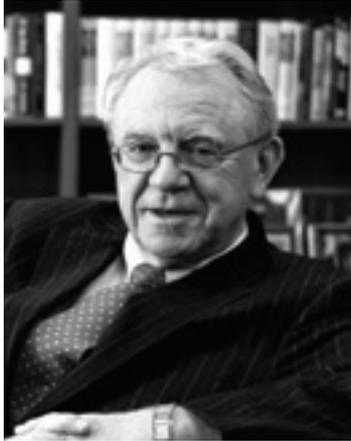
**Herbert Pardes, M.D.**
President of the Scientific Council

Executive Vice Chairman of the Board of Trustees
NewYork-Presbyterian Hospital

"The Young Investigator Grant program is the hallmark program of the Brain & Behavior Research Foundation and represents the intersection of cutting-edge brain and behavior research and innovation. These grants enable outstanding scientists to pursue bold new ideas to answer an important question or help identify potentially game-changing targets for treatment. The awards function as seed funding for new directions which would otherwise be highly unlikely."

**Jeffrey Borenstein, M.D.**
President & CEO

"We are proud to support the work of these young scientists, who will apply powerful new technologies and insights to understanding, treating and curing mental illness. Past recipients of our Young Investigator Grants include three neuroscience superstars [on page 9] who have researched and created such game-changing discoveries as deep brain stimulation for treatment resistant depression, transcranial magnetic stimulation (TMS), and the development of optogenetics."

# Advancements in Mental Health Research from Initial Young Investigator Grant Support:

## DEEP BRAIN STIMULATION

**Dr. Helen Mayberg,** Professor of Psychiatry and Behavioral Sciences and Neurology at the Emory University School of Medicine, received her first Young Investigator Grant more than 20 years ago and with it she pioneered the use of PET and MRI functional imaging to investigate brain changes in depressed patients. With the further support of a Independent Investigator Grant in 1995, she identified a key locus of pathology in depression (the subcallosal cingulate or Brodmann Area 25). In 2002, with a Distinguished Investigator Grant, she led breakthrough research when she piloted the use of deep brain stimulation to target this Area 25' to treat patients with treatment-resistant depression.

Since her initial Young Investigator Grant funded in 1991 she has received related subsequent funding exceeding $8.5 million or more than 140 times her original Grant amount.

## TRANSCRANIAL MAGNETIC STIMULATION

**Dr. Mark George,** Distinguished Professor of Psychiatry, Radiology and Neuroscience at the Medical University of South Carolina developed transcranial magnetic stimulation (TMS) as an alternative to electroconvulsive therapy in treatment-resistant depression. FDA-approved in 2008, TMS does not induce seizures as ECT does, but does exploit the fact that the brain is an electrical organ: it responds to electrical and magnetic stimulation to modulate brain circuits and change brain activity. In 1995 Dr. George was unable to get NIMH funding for TMS, and it was because of the support of a Young Investigator Grant that he was able to pursue this work.

Following his initial Grant, numerous NIMH, and Department of Defense and V.A. awards valued at several millions of dollars furthered the development of this now FDA-approved treatment.

## OPTOGENETICS

**Dr. Karl Deisseroth,** D.H. Chen Professor of Bioengineering and of Psychiatry and Behavioral Sciences and the Howard Hughes Medical Institute Investigator at Stanford University, used a Young Investigator Grant in 2005 for the development of what he has termed 'optogenetics.' Optogenetics was heralded by the White House, in the announcement of their BRAIN Initiative, as one of the "landmark discoveries that now create the opportunity to unlock the mysteries of the brain … for instance, by combining advanced genetic and optical techniques [optogenetics], scientists can now use pulses of light to determine how specific cell activities in the brain affect behavior." Dr. Deisseroth has made the technology openly available for use by researchers and it is in use at thousands of laboratories around the world.

Since his initial Young Investigator Grant funding in 2005, he has received more than $3 million in related research funding valued at more than 50 times the original grant amount.

# The 2017 Young Investigator Grantees

The Foundation is pleased to announce $13.6 million in 196 new two-year grant awards to support the work of promising young scientists with innovative ideas in mental health research.

The grants for 2017 address exceptional research questions across diagnostic categories, from schizophrenia and depression to anxiety, PTSD, autism spectrum disorder, ADHD, addiction and bipolar disorder, among others.

We have seen an increase in the number of grants supporting research that we classify and describe as "Mental Illness-General" and "Multiple Disorders." This is due to the fact that because of recent advances in research which show that causality and mechanisms involved in various disorders often cross traditional diagnostic boundaries. In order to capture a sense of the subjects of this large number of grants we have provided subject areas for Mental Illness-General and subjects plus the disorders they may apply to for Grants labeled as Multiple Disorders.

- About 73 percent of the projects funded are basic research, the wellspring of innovation in brain research as in all sciences.

- About 14 percent of the 2016 grants fund projects that specifically aim to develop next-generation therapies.

- About 10 percent of the projects funded are diagnostic tools/early intervention that aim to prevent brain and behavior disorders.

- About three percent fund the development of new technologies that will power both basic research and new developments in the clinic.

On the following pages you will find our 2017 Grantees listed by illness and subtyped under these categories:

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**RESEARCH CATEGORIES**

Basic Research (144 Grants)
To understand what happens in the brain to cause mental illness

Early Intervention/Diagnostic Tools (20 Grants)
To recognize early signs of mental illness and treat as early as possible

New Technologies (6 Grants)
To advance or create new ways of studying and understanding the brain

Next Generation Therapies (26 Grants)
To reduce symptoms of mental illness and ultimately cure and prevent brain and behavior disorders

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We are very grateful to all of our donors
for their continuous support
in the careers of these young scientists.

# ADDICTION

**Brian A. Anderson, Ph.D.,** Texas A&M University, will follow up on prior research in which he identified a phenomenon called value-driven attention, which has implications for understanding and treating drug addictions. Value-driven attention refers to the tendency to turn one's attention to a stimulus that has previously come with a reward, despite attempts to ignore it. Dr. Anderson seeks to better distinguish among learned factors that give rise to such attentional biases, and connect them to specific processes in the brain.

Basic Research

**Kasia Maria Bieszczad, Ph.D.,** Rutgers University, aims to determine whether specific changes within the cortex are linked to cue-triggered drug-seeking and related behaviors. Cues such as sounds can be central to an initial experience of overwhelming stress or taking drugs, creating an association between the cue and the desire to use drugs. Working in mice, Dr. Bieszczad will examine how altering the levels at which genes are expressed affects the ability to learn and forget specific drug-associated sound cues.

Basic Research

**Shaunna L. Clark, Ph.D.,** Virginia Commonwealth University, will explore patterns of gene expression in the brains of patients with alcohol dependence. Dr. Clark aims to comprehensively map the epigenetic marks, which regulate the level at which genes are expressed, in the postmortem brains of alcohol dependent patients. The study will focus on prefrontal cortex, a brain region involved in many aspects of cognition.

Basic Research

**Lindsay Mitchell De Biase, Ph.D.,** National Institute on Drug Abuse (NIDA/NIH), will investigate the role of brain cells called microglia in the response to drugs of abuse. The ventral tegmental area (VTA) of the brain is a key producer of dopamine, a chemical released as a signal of rewarding expe-

riences, including drug use. To determine whether microglia regulate this brain region's response to drugs, Dr. Mitchell De Biase study their activity in mice after exposure to cocaine.

Basic Research

**Tristen Kimiko Inagaki, Ph.D.,** University of Pittsburgh, will examine the impact of naltrexone, an opioid blocker prescribed during recovery from addiction, on social connection and brain function. She notes that maintaining healthy relationships can be key to recovery and that feeling less connected socially, which can be a side effect of blocking opioids, may increase risk for relapse. Using fMRI, she will compare patients taking naltrexone and placebo as they complete tasks designed to elicit feelings of social connection with their loved ones. Social behavior outside the scanner will also be tracked. Results could illuminate mechanisms underlying feelings of social connectedness and inform the development of better treatment plans for those recovering from addiction.

Next-Generation Therapies

**Jee Hyun Kim, Ph.D.,** Florey Neuroscience Institutes, University of Melbourne, Australia, hopes to explore what molecular changes occur in the brain to make methamphetamine abuse a significant problem in adolescents. Adolescents tend to be resistant to current addiction treatments and are more likely to relapse than adults. Dr. Kim will build on previous research demonstrating that adolescents who take methamphetamines have reduced expression of the gene SLC18A1, which produces a protein called VMAT1 in the brains of both rodents and humans. The goal of the study is to investigate whether increasing levels of VMAT1 in the rodent brain could protect against escalating methamphetamine intake in adolescent and adult rats.

Basic Research

**Drew Donovan Kiraly, M.D., Ph.D.,** Icahn School of Medicine at Mount Sinai, will examine the potential impacts of the gut microbiome on cocaine addiction, building on earlier research suggesting links between changes in the gut's microbes and several mental illnesses, including depression and anxiety. Dr. Kiraly seeks to discover whether or when changes to the gut microbiome influence drug-craving and -

seeking behaviors, as well as whether the effects of the micro-biome on microglia, the immune cells of the brain, are key to the microbiome's impact on cocaine addiction behavior.

IDGI Basic Research

**Xiaofan Li, Ph.D.,** Icahn School of Medicine at Mount Sinai, hopes to examine how psychostimulant drugs such as methamphetamine alter a reward circuit in the brain thought to be involved in addictive behavior. The circuit involves dopamine neurons in a part of the brain called the ventral tegmental area. Using a mouse model of methamphetamine addiction, Dr. Lithe seeks to learn whether inhibition of this addiction circuit is weakened by repeated drug use, and whether inhibition in this area could be altered to slow the development of addiction.

IDGI Basic Research

**Tiffany Love, Ph.D.,** University of Utah, will be exploring how male and female hormones can influence social and non-social information processing in people with alcohol use disorder. Social functioning is often poor in those with the disorder, and may contribute greater symptom severity, worse treatment outcomes and an elevated risk for suicide. The study will analyze how gender differences in social information processing may contribute to the differences in alcohol use disorder in men and women—a question that has not been adequately explored despite evidence suggesting that men and women experience the disorder differently.

IDGI Basic Research

**Kate McDonnell-Dowling, Ph.D.,** Tufts University, studies the long-term effects of early-life exposure to aggressive confrontations and abuse on susceptibility to drug seeking and drug use in adulthood, specifically whether this exposure may have neurological consequences that lead to enhanced drug seeking and consumption. Mice will be exposed to confrontation with unfamiliar mice during prenatal, post-natal, and adolescent life stages. The goal is to determine what neuroadaptations that encourage drug use may arise from aggression during each stage. The research also will investigate whether re-exposure can exacerbate drug seeking and use in adulthood.

IDGI Basic Research

**Elizabeth Genevieve Mietlicki-Baase, Ph.D.,** State University of New York (SUNY), University of Buffalo, hopes to learn more about the role of an understudied part of the brain called the nucleus of the solitary tract, and how it may relate to reward-seeking behavior and drug addiction. The study will focus on a protein receptor at this site called GLP-1R, with experiments to test whether molecular signaling at this receptor is related to cocaine-seeking behavior in rats. Additionally, given that "binge-like" food intake increases cocaine seeking, the study will test whether binge-like consumption alters the expression of GLP-1R.

IDGI Basic Research

**Hyung Wook Nam, Ph.D.,** Louisiana State University Health Sciences Center, hopes to expand the data available on potential biomarkers for alcohol craving across a racially diverse sample. To this end, the proposed study will include 50 percent African-American patients with alcohol use disorders. The goal is to examine the blood for metabolites related to the enzyme glutamine synthetase, a biomarker that has been associated with a positive response to the anti-alcohol abuse drug acamprosate. The study will also look for patterns in abnormal connectivity in the brain during its "resting state," which has been linked to conditions such as craving and anxiety.

IDGI Diagnostic Tools/Early Intervention

**James Mark Otis, Ph.D.,** University of North Carolina at Chapel Hill, hopes to learn more about changes in the brain's prefrontal cortex that underlie compulsive drug seeking and relapse. Although prefrontal cortex alterations are the hallmark of addiction, little is known about the exact neural circuits that are modified. Dr. Otis will examine the activity of three key subpopulations of neurons in this area of the brain in a rodent model of drug seeking. Earlier research shows that these three subpopulations play supporting or opposing roles in normal reward-seeking behavior, which has been linked to addiction. The new study will determine how each group of neurons is engaged by drug-seeking cues over time.

IDGI Basic Research

**Michael P. Saddoris, Ph.D.,** University of Colorado, Boulder, will examine a potential learning strategy for helping people with addiction resist stress-related relapse. Stress can provoke drug cravings among dependent individuals. Dr. Saddoris will test whether learning how to escape a stressful experience will enable addicted rats to become less attracted to cocaine. He predicts that stress learning will reduce cocaine use by regulating activity in the nucleus accumbens, a brain region crucial for the reward system and linked to addiction.

🧬 Basic Research

**Fair Maclaren Vassoler, Ph.D.,** Tufts University, will explore a novel treatment strategy for addiction and other mental illnesses. The method focuses on chemical messengers known as miRNAs that control gene expression in cells and have been implicated in many psychiatric illnesses. The work aims to develop a strategy to deliver miRNAs into patients with addiction and mental illnesses to modulate the expression of specific genes.

🧬 Next-Generation Therapies

**Leora Yenikoff, Ph.D.,** City University of New York, College of Staten Island, will study the development of dopamine neurons, a class of cells that is essential in reward, learning and cognition. Taking advantage of new technology (known as the proximity ligation assay), Dr. Yenikoff will comprehensively examine the development and plasticity of dopamine synapses, focusing on the adolescent period and the role of drugs of abuse, in particular. The work will assess how stimulants affect the connections between neurons in an effort to refine and improve existing addiction treatments.

🧬 Basic Research

**Panos Zanos, Ph.D.,** University of Maryland, Baltimore, will explore the potential of a ketamine derivative, called hydroxynorketamine, as a treatment for addiction and disorders associated with it. Many recovering addicts suffer from mood disorders, including increased anxiety and social withdrawal, which make relapse more likely. Dr. Zanos hopes that the ketamine-like drug will prevent these symptoms during opioid withdrawal, improving the likelihood of successful recovery.

🧬 Next-Generation Therapies

# ADHD
*Attention-Deficit Hyperactivity Disorder*

**Michelle Marie Downes, Ph.D.,** University College Dublin, Ireland, seeks to identify potential early markers of poor attention control in infants at high genetic risk for ADHD. Dr. Downes will study the brain development of infants whose parent or siblings have a diagnosis of ADHD in search of markers that may aid early diagnosis.

🧬 Diagnostic Tools/Early Intervention

**Claudia Amorim Lopes, Ph.D.,** Harvard Medical School, will be creating cerebral organoids—"mini-brains" grown in 3D culture--to investigate neurodevelopmental changes that may be related to the ADHD brain. The organoids will be generated from cells taken from both ADHD patients and their healthy siblings, and coaxed into stem cells that can grow into a model of the brain's cortex. The process will allow Dr. Lopes to study molecular and cellular differences in cortex growth and development between ADHD and healthy brains, and to pinpoint any differences that relate to reduced brain volume and delayed maturation and formation of neural connections, all of which have been linked to the disorder.

🧬 New Technologies

**Timothy Spellman, Ph.D.,** Weill Cornell Medical College, hopes to identify connections in the brain that allow us to focus attention on the most important stimuli, an ability that is sometimes impaired in psychiatric illness, ADHD. Using a new brain imaging technique called light field microscopy, Dr. Spellman will look at prefrontal cortex, known to coordinate attention, to identify and then control neuronal circuits that direct attention. He hopes his findings will lay the groundwork for circuit-specific interventions to treat attention deficits in different disorders.

🧬 Basic research

# ANXIETY

**Gaurav Bedse, Ph.D.,** Vanderbilt University Medical Center, will examine the interactions between two different potential drug types. Both endocannabinoid degradation inhibitors and NMDA antagonists are currently being explored as treatments for anxiety. Using mice, Dr. Bedse aims to verify previous results suggesting that simultaneous administration of such drugs have synergistic anti-anxiety effects.

Next-Generation Therapies

**Kevin Thomas Beier, Ph.D.,** Stanford University, seeks a better understanding of the brain circuitry involved in experience-triggered anxiety. Evidence suggests that some dysfunctional brain circuitry is shared between anxiety and disorders with which it often co-occurs, such as drug addiction. Indeed, mice that model cocaine withdrawal display anxiety behaviors. By observing the behaviors of mice experiencing cocaine withdrawal and measuring changes within their brains, Dr. Beier hopes to identify specific differences that arise in animals that develop anxiety.

Basic Research

**Laura Bevilacqua, M.D., Ph.D.,** Icahn School of Medicine at Mount Sinai, will test the effects of nasal administration of an experimental anti-anxiety drug called neuropeptide Y (NPY) on threat response. To further clarify NPY's effects and provide critical information on proper dosage, Dr. Bevilacqua's team will observe healthy volunteers' performance in a laboratory-based threat task.

Next-Generation Therapies

**Nadeeka Nirupama Dissanayaka, Ph.D.,** University of Queensland, Australia, will examine the feasibility of using smart devices and virtual reality as a new therapy for anxiety disorders in Parkinson's disease patients. Smart watches will deliver biofeedback alerts based on measurements such as heart rate while patients use virtual reality applications at home on their smart phones. Dr. Dissanayaka hopes that

this will be a more accessible, tolerable, and effective therapy for patients suffering from both of these disorders, a group which comprises the majority of PD patients.

Next-Generation Therapies

**Oriel Feldmanhall, Ph.D.,** Brown University, endeavors to elucidate brain networks associated with risky social decision-making and their link with heightened vulnerability to anxiety disorders in adolescence. Dr. Feldmanhall predicts that abnormal development of a brain region called the dorsolateral prefrontal cortex (dlPFC) will facilitate hyper-reactivity to events that are socially and emotionally charged. The team will test these brain-behavior relationships and their association with increased anxiety levels.

Basic Research

**Kathryn M. Harper, Ph.D.,** University of North Carolina at Chapel Hill, will investigate how a molecule involved in the brain's immune system influences anxiety. Known as CCL2, this molecule binds to receptors found on brain cells in a region implicated in many forms of anxiety, including that induced by alcohol withdrawal. Dr. Harper aims to determine whether CCL2 contributes to anxiety-like behavior in mice by inhibiting the activity of this brain region, called the central amygdala.

Basic Research

**Jennifer Ann Honeycutt, Ph.D.,** Northeastern University, will develop a rat model to test the links between early life stress and its impact on an important communication pathway that regulates the response to anxiety-provoking events in children's brains. The study by Dr. Honeycutt will use a rat model of early life stress to learn more about critical changes in the connection between the brain's amygdala and prefrontal cortex in response to early life stress, and track any changes in anxious behavior as a result.

Basic Research

**Zheng Jiang, Ph.D.,** Johns Hopkins University, notes that a number of cognitive functions including anxiety, alertness, and general mood are impacted by light exposure. Using mouse models, Dr. Jiang will look at the role of cells in the retina called intrinsically photosensitive retinal ganglion cells

(ipRGCs) on inducing behaviors related to anxiety. He hopes to better understand the function of these cells in activating different brain areas related to anxiety and triggering related behaviors.

◫ Basic Research

**Antonia N. Kaczkurkin, Ph.D.,** University of Pennsylvania, is studying how differences in the way men and women experience anxiety disorders may be related to sex differences in brain development. She will first compare "at this moment" data reported by healthy youth and those with anxiety disorders, in a process called ecological momentary assessment (EMA), to look for sex differences in the frequency and intensity of anxiety symptoms. The team will also collect long-term neuroimaging data on to investigate how anxiety symptoms measured by EMA might relate to abnormalities in brain development. The goal is to identify biological markers that could be used to identify youth at risk for anxiety disorders.

◫ Diagnostic Tools/Early Intervention

**Johannes Kohl, Ph.D.,** Harvard University, will examine the role that a group of neurons called MPOA-Gal may play in reducing a mother's anxiety directly after giving birth. The goal is to examine how this circuit might contribute to postpartum anxiety, and whether it may represent a target for future therapies. In mice, Dr. Kohl will test the hypothesis that the activity of these neurons increases during pregnancy and helps to scale down anxiety behaviors in late pregnancy and immediately after birth, in preparation for parenting behavior. His team will also interfere with this circuit in mice, to see if it will generate postpartum anxiety in the animals.

◫ Basic Research

**Indira Mendez-David, Ph.D.,** Université Paris-Sud 11, France, will take a closer look at the serotonin receptor 5-HT4R and its targets in a part of the brain called the dorsal raphe nucleus (DRN), for their potential as a target for a fast-acting anxiety drug. SSRI antidepressant drugs are often prescribed to treat anxiety disorders, but more specific agents are sought. This study seeks to confirm that activation of 5-HT4R is necessary to generate a fast-acting anti-anxiety

effect and to show that this effect is linked to neurochemical changes in the DRN. Dr. Mendez-David will stimulate and silence neural links traveling to the DRN to determine if these changes have either neurochemical or anti-anxiety behavioral effects in mice.

◫ Basic Research

**Judith K. Morgan, Ph.D.,** University of Pittsburgh, will evaluate neural differences in response to social stimuli in preschool children who have high levels of shy and inhibited behavior in new situations. This trait has been linked to elevated rates of social anxiety disorder and other mental illnesses later in life. The study will use a non-invasive imaging method to observe the brains of children with this trait, along with their parents, as they engage in social interactions that require social flexibility, or the ability to update goal-directed behaviors as social situations change.

◫ Basic Research

**Michelle Pelcovitz, Ph.D.,** Weill Cornell Medical College, will examine whether virtual reality (VR) experiences can be used successfully in treatments for social anxiety disorder in adolescents. The usual treatment for this disorder is extinction therapy, in which a person is exposed repeatedly to threatening stimuli in a safe environment with the goal of decreasing the fear response. Dr. Pelcovitz will test whether VR technology would be a feasible way to deliver extinction therapy to a group of adolescents and young adults diagnosed with social anxiety. The study will include tests to see if the VR experience provides the same level of arousal as an anxiety-provoking situation, and whether VR exposure can reduce symptoms of social anxiety with the same effectiveness as traditional extinction therapy.

◫ Next-Generation Therapies

**Joanna Spencer-Segal, M.D., Ph.D.,** University of Michigan, will investigate the brain regions that make people more vulnerable to developing mood disorders after they experience severe illness. Dr. Spencer-Segal will look at mice that have recovered from a serious infection, or sepsis, which often leads to anxiety following recovery. Her team expects

to find that this anxiety corresponds to changes in neuronal activity within the ventral hippocampus. They will test whether manipulating activity in this brain region affects anxiety symptoms in mice.

IDCI Basic Research

**Chad Michael Sylvester, M.D., Ph.D.,** Washington University, hopes to identify neural networks in newborns that predict anxiety later in life. Dr. Sylvester will study interconnected regions in the brain, comparing infants who are at high risk of developing an anxiety disorder with those that are at low risk. This research could help in the design of new early treatments aimed at a time when neural networks are easily changed.

IDCI Basic Research

# ASD
## *Autism / Autism Spectrum Disorder*

**Konstantinos Ampatzis, Ph.D.,** Karolinska Institute, Sweden, will work to better understand the underpinnings of autism spectrum disorders (ASDs) in the brain by studying a region called the cerebellum. While it is most commonly associated with its role in coordinating muscle movements, the cerebellum is also linked to cognition, emotions, and psychiatric illness. To elucidate the cerebellum's role in ASDs, Dr. Ampatzis will examine results from functional imaging experiments as well as anatomy, genetics, and other factors.

IDCI Basic Research

**Adriaan Johannes Boender, Ph.D.,** Emory University, will explore the connection between the hormone oxytocin and autism spectrum disorders (ASD) through studies of prairie voles. These rodents form life-long pairs and display other human-like social behaviors, making them a valuable tool for studying the causes of the dysfunctional social behavior typical of ASD. By altering the genes involved in using oxytocin, Dr. Boender hopes to shed light on how genes regulate social behavior and can cause ASD.

IDCI Basic Research

**Luke Bury, Ph.D.,** Case Western Reserve University, will harness the power of a new technology known as cerebral organoids to study the link between autism spectrum disorders (ASD) and macrocephaly, or overgrowth of the brain. Cerebral organoids are three-dimensional clusters of cells that mimic many aspects of human brain development. Using cells attained from ASD patients who also display macrocephaly, Dr. Bury will develop cerebral organoids with the potential to shed light on the aspects of brain development that give rise to both disorders.

IDCI New Technologies

**Dhananjay Huilgol, Ph.D.,** Cold Spring Harbor Laboratory, will explore the mechanisms that control neuronal diversity during brain development. Dr. Huilgol will analyze the morphology, organization, and connectivity of projection neurons that facilitate communication throughout the brain. This research could provide invaluable insights into the organization of the brain's cortex and the etiology of autism spectrum disorders, which are characterized by abnormal connectivity and brain overgrowth.

IDCI Basic Research

**Arkady Khoutorsky, Ph.D.,** McGill University, Canada, will study the role that the integrated stress response (ISR) pathway may play in dysregulated proteins involved in brain disorders including autism. The ISR pathway consists of a collection of molecular changes that cells undergo to cope with environmental stresses, and is a key regulator of protein synthesis. Problems with protein synthesis in brain cells have been linked to autism. Dr. Khoutorsky will examine whether disruptions in the ISR pathway are behind protein alterations in the brains of mice that have a model of Fragile X syndrome (a genetic disorder with some autism-like symptoms), and whether these alterations contribute to brain abnormalities and impaired behavior.

IDCI Basic Research

**Hui-Chen Lu, Ph.D.,** George Washington University, hopes to discover why different genetic defects in Rett syndrome and MECP2 duplication syndrome lead to the same kinds of social behavior problems. The findings could shed light on how social deficit—one of the core ASD symptoms—may be produced by a variety of molecular alterations. The study will explore the consequences of loss of function in the MECP2 gene (as in Rett) and multiplication of the gene

(as in MECP2 duplication) to determine how these opposite defects lead to shared abnormalities in the brain circuits associated with social deficit.

IIDGII Basic Research

**Annabella Pignataro, Ph.D.,** IRCCS Fondazione Santa Lucia, Italy, will explore whether insufficiency of a gene called AMBRA1 in mice can lead to ASD-like impairments in certain brain circuits in female mice, and whether these impairments can be reversed. The research could shed light on possible reasons for differences in the risk of the disease between males and females. The gene is involved in creating balance between neural activation and inhibition, and disruption of this balance can underlie dysfunctional circuits in ASD.

IIDGII Basic Research

**Randall Jeffrey Platt, Ph.D.,** ETH Zurich, Switzerland, hopes to compare the hundreds of known ASD-associated genetic mutations in one experiment, to better understand how these mutations may be linked biologically to the symptoms of ASD. The experiment, using the gene-editing technology called CRISPR, will create these mutations directly in the developing mouse brain within cells that are thought to be responsible for the underlying biological cause of ASD.

IIDGII Basic Research

**Nathaniel Snyder, Ph.D., M.P.H.,** A.J. Drexel Autism Institute, hopes to uncover the origins of neurodevelopmental orders that begin in the womb. Dr. Snyder will look at meconium, an infant's first bowel movement, to assess the metabolism of molecules that may give rise to autism spectrum disorders in developing children. In particular, his team will test whether androgen steroids correspond to the risk for autism, and if that risk is in turn reduced by estrone and neurosteroid hormones.

IIDGII Basic Research

**Jason J. Yi, Ph.D.,** Washington University School of Medicine, will investigate the function of a protein known as UBE3A in autism. Excessive UBE3A activity has been linked with one of the most common forms of autism in children. Dr. Yi will explore how UBE3A is regulated and how its excessive activity affects the chemistry of proteins in the brain, in the hope of understanding the molecules and mechanisms that lead to the development of autism.

IIDGII Basic Research

**Eunice Y. Yuen, Ph.D.,** Yale University, will study the role of inhibitory GABA neurons in autism spectrum disorder. In patients with ASD, these neurons are highly overproduced, but it is unknown what role they play in the disorder. Dr. Yuen will use organoids derived from autistic children and their parents to understand how the development of GABA neurons differs. The results should lay the foundation for future mechanistic studies using human organoids and may identify potential drug targets in autism.

IIDGII Basic Research

# BIPOLAR DISORDER

**Stefano Comai, Ph.D.,** San Raffaele Vita-Salute University, Italy, aims to examine whether regulation of melatonin, a hormone that influences brain activity, may be a viable treatment option for bipolar disorder. Melatonin is involved in the circadian system, which is key to behaviors that are regularly performed on a 24-hour cycle and is known to be extensively disrupted in bipolar disorder patients. Dr. Comai will test the effects of pharmacologically altering melatonin usage in the brains of mice and examine the link between melatonin levels and bipolar disorder in humans.

IIDGII Next-Generation Therapies

**Daniel Hochbaum, Ph.D.,** Harvard University, will look for new ways to study mania, a characteristic symptom of several mental illnesses, most notably bipolar disorder. Mania shares many symptoms with hyperthyroidism, a disease characterized by excessive levels of thyroid hormone production. Since hyperthyroidism is easier to study in mice, Dr. Hochbaum proposes a study that will investigate gene alterations in normal and hyperthyroid mice to identify neurons that are perturbed by thyroid dysfunction, ultimately correlating these changes with specific neural circuits.

IIDGII Basic Research

**Liping Hou, Ph.D.,** National Institute of Environmental Health Sciences, hopes to learn more about the genetic basis for responding to lithium treatment for bipolar disorder. Lithium is a first-line treatment for the illness, but patients vary considerably in their response to the treatment. The study will build on a previous large-scale genome-wide association study of lithium response, adding 1500 genetic samples within two years. The analysis will identify genes that affect lithium response, which could be used to learn more about how lithium works in the brain and to help patients and their physicians determine whether lithium is likely to beneficial in a treatment plan.

Basic Research

# BORDERLINE PERSONALITY DISORDER

**Keith Bush, Ph.D.,** University of Arkansas for Medical Sciences, will employ a new technology known as real-time functional magnetic resonance (rtfMRI) imaging to test the effects of images on emotional regulation, which is dysregulated in borderline personality disorder (BPD) and other disorders ranging from depression and anxiety to PTSD and substance abuse. Human volunteers will look at emotionally charged images while researchers monitor their brain activity using rtfMRI. Dr. Bush aims to reveal a neural mechanism underlying the tactic of instructing psychiatric patients to focus on neutral or positive thoughts, one of the most popular strategies in cognitive behavioral therapy, which is frequently used in BPD.

New Technologies

# DEPRESSION

**Florent Barthas, Ph.D.,** Yale University, hopes to illuminate the brain circuitry underlying reward-related symptoms observed in depression. A brain region called the prelimbic cortex is a central node for the brain's reward circuitry. Dr. Barthas will image this region of the brain in mice as they perform a reward-driven task in order to gain a better understanding of how the prelimbic cortex responds to chronic stress.

Basic Research

**Tjeerd Willem Boonstra, Ph.D.,** University of New South Wales, Australia, will investigate how ketamine treatment alters brain function in patients with depression. The study will examine the brain activity of patients with treatment-resistant depression before, during, and after treatment to better understand the changes that ketamine causes. Dr. Boonstra hopes that the insights from this work will aid the identification of patients most likely to benefit from treatment.

Next-Generation Therapies

**Julia Brill, Ph.D.,** Johns Hopkins University, seeks a better understanding of the mechanism through which estrogen-blocking breast cancer therapies increase women's risk of depression. One such breast cancer therapy is called letrozole, and has been shown to reduce the amount of connections extending from pyramidal neurons, a type of brain cell. By administering letrozole to mice and studying the changes that occur in these brain cell connections, Dr. Brill hopes to shed light on the ways in which this type of therapy affects the basic properties of pyramidal neurons.

Basic Research

**David Bulkin, Ph.D.,** Cornell University, will use genetic tools to probe a brain circuit in a region called the lateral habenula, which has been linked to depression in both rodents and humans. Working in mice, Dr. Bulkin will stimulate neurons in the lateral habenula and monitor brain activity while the animals are awake and behaving. Evaluation of the animals' performance on chronic stress tests will also aid in clarifying how stimulation of the lateral habenula affects depression.

Basic Research

**Lauren M. Bylsma, Ph.D.,** University of Pittsburgh, will investigate how the community of microscopic organisms that inhabit our digestive systems, known as the gut microbiome, may affect depression risk. Noting that depression rates spike during adolescence, the Dr. Bylsma will characterize the microbiomes of adolescents with depression and with high familial risk of depression and compare with profiles of healthy adolescents. This project will also link stress and reward systems in the brain with microbiome characteristics in humans.

Basic Research

**Maithe Arruda Carvalho, Ph.D.,** University of Toronto, Canada, is interested in how the maturation of brain circuits may contribute to adolescents' susceptibility to stress and depression. Brain regions such as the nucleus accumbens mature during adolescence, when new depression cases often emerge. By examining the changes that occur within these brain regions in mice as they age and respond to stress, Dr. Carvalho hopes to obtain knowledge that will ultimately help optimize clinical therapies for young people with depression.

Basic Research

**Basar Cenik, M.D., Ph.D.,** University of Texas Southwestern Medical Center at Dallas, will investigate whether certain sterols, fat molecules similar to cholesterol, can be biomarkers in depression. Previously Dr. Cenik revealed changes in the levels of two types of sterols in the blood correlated with depressive symptoms. Postmortem brains from people diagnosed with depression will be examined to determine whether the same changes are also present in the brain.

Diagnostic Tools/Early Intervention

**Alexandra Elyse D'Agostino, Ph.D.,** Stony Brook University School of Medicine, is interested in the potential of an anti-inflammatory drug called celecoxib as a treatment for major depressive disorder (MDD). The team will first investigate brain inflammation as an underlying issue in depression and test whether celecoxib reduces the severity of such inflammation in MDD patients. Dr. D'Agostino hypothesizes that celecoxib treatment will reduce inflammation in several brain regions implicated in depression, thereby reducing patients' depressive symptoms.

Next-Generation Therapies

**Elena Goetz Davis, Ph.D.,** Stanford University, will look to the epigenome, molecular marks that regulate the activity of specific genes, to better understand how stress early in a girl's life contributes to depression vulnerability. Focusing on a type of epigenetic mark called DNA methylation, Dr. Davis will examine this biomarker in female participants in on ongoing study. The team will measure how DNA methylation patterns change in response to stressful versus protective environments during early life and puberty, and how this may predict the onset of major depressive disorder in adolescence.

Diagnostic Tools/Early Intervention

**Zhi-De Deng, Ph.D.,** National Institute of Environmental Health Sciences (NIEHS/NIH), aims to develop seizure therapy for depression that avoids the serious side effects of existing electroconvulsive therapy. Dr. Deng plans to achieve these results by using computational modeling to direct multi-electrode configurations that provide targeted and individualized dosing. This project will test the technology in a proof-of-concept human study.

Next-Generation Therapies

**Sam Emaminejad, Ph.D.,** University of California, Los Angeles, will implement a non-invasive, wearable diagnostic device that measures a panel of biomarkers for major depressive disorder (MDD) symptoms. The device employs fully integrated wearable sweat extraction and analysis technology to measure pro-inflammatory cytokines and neuropeptide Y, both biomarkers of MDD. Dr. Emaminejad aims to address the challenges currently presented by factors such as varying sweat secretion rates.

▨▨ Diagnostic Tools/Early Intervention

**Lorna Alice Farrelly, Ph.D.,** Icahn School of Medicine at Mount Sinai, seeks a more detailed understanding of the role that serotonin, a signaling molecule in the brain, plays in major depressive disorder (MDD). Dr. Farelly will study serotonylation, a process by which serotonin bonds certain protein molecules in cells. Serotonylation is known to be significantly altered in certain brain areas of MDD patients and completely reversed by antidepressant treatment. Using rodent models and postmortem brains from MDD patients, she will investigate the effects of serotonylation when it acts on molecules called histones, which aid in the packaging of DNA in cells.

▨▨ Basic Research

**Tracy Lee Gilman, Ph.D.,** University of Texas Health Science Center at San Antonio, will investigate the ability of a structure called the plasma membrane monoamine transporter (PMAT) to regulate depressive and other neuropsychiatric behaviors. Found in brain cells, the PMAT is transports the brain signaling molecules dopamine and serotonin, and is heavily implicated in depression. Using mice, Dr. Gilman aims to show how partial and full reduction of PMAT function affects relevant behaviors and response to antidepressants.

▨▨ Basic Research

**Ronald Gerardo Garcia Gomez, M.D., Ph.D.,** Brigham and Women's Hospital and Harvard University, will evaluate the effects of a new therapy for major depressive disorder (MDD) that employs stimulation of the vagus nerve, a key regulator of mood and emotional stress. Existing therapies that use this approach require invasive surgery to implant electrodes. Dr. Gomez strives to overcome this obstacle with a non-invasive vagus nerve stimulation technique that applies electrical pulses over the skin of the outer ear. The team will administer this therapy to MDD patients to determine its effectiveness in reducing depressive symptoms.

▨▨ Next-Generation Therapies

**Stephanie Marie Gorka, Ph.D.,** University of Illinois at Chicago, will focus on young adults in a study of the link between intolerance of uncertainty in one's environment and risk for depression. The team will measure physiological and neural traits to ascertain onset and changes in depressive symptoms, positive emotionality, and anhedonia over the course of at least one year. Dr. Gorka hopes that these results may help in identifying who is vulnerable to major depressive disorder to facilitate active detection, prevention, and treatment.

▨▨ Diagnostic Tools/Early Intervention

**Elseline Hoekzema, Ph.D.,** Leiden University, Netherlands, has studied how pregnancy brings about consistent and long-lasting changes to the human brain. Some of these changes may be linked to postpartum depression. Although the disorder is the most common complication of pregnancy and childbirth, few studies have examined its neural basis. Dr. Hoekzema will investigate possible relationships between pregnancy-related structural brain changes and the development of postpartum depressive symptoms. The study will also identify hormonal or neural biomarkers that may signal a predisposition for postpartum depression.

▨▨ Diagnostic Tools/Early Intervention

**Raquel Iniesta, Ph.D.,** King's College London, UK, will develop new machine learning algorithms that combine genetic, demographic, and clinical information to better predict antidepressant treatment outcomes at the individual level. This research could result in useful predictive models to guide clinicians in selecting more effective treatments for patients with depression, solving a major challenge that is posed by individual variation in treatment response and an inability to predict who will respond to which treatments.

▨▨ Diagnostic Tools/Early Intervention

**Orna Issler, Ph.D.,** Icahn School of Medicine at Mount Sinai, will investigate how epigenetic mechanisms, which alter the expression of genes, contribute to depression. Dr. Issler will focus on long non-coding RNAs (lcRNAs). After identifying depression-related lncRNAs from post-mortem samples and studying their mechanisms of action in mouse models, she will isolate lncRNAs that could be used as potentials biomarker to test for depression in humans. Taken together, this research could provide a more complete view of the function of lcRNAs in depression and reveal new targets for improved treatment.

▥ Basic Research

**Chung Sub Kim, Ph.D.,** University of Texas at Austin, is working to discover the cellular mechanisms behind the ability of the drug ketamine to rapidly relieve symptoms of depression, including treatment-resistant depression. The goal is to develop new drugs that deliver the same fast-acting effects with fewer side effects than ketamine. Dr. Kim will study the effects of ketamine in rats and in lab samples of a part of the brain called the hippocampus to determine whether the drug may counteract the effects of neural inhibition associated with depression-like symptoms.

▥ Basic Research

**Daphne Jennifer Korczak, M.D., MSc,** University of Toronto, Canada, will investigate the relationship between vascular function, cardiovascular disease risk and depression in adolescents. The goal is to observe the potential origin of cardiovascular disease in people with depression, as it is the leading cause of death for people with the disorder. The study will compare arterial stiffness, obesity, blood pressure, insulin levels, inflammation and other markers of disease in adolescents with and without a depression diagnosis. The findings could inform new interventions that target immune-related factors in the treatment of depression.

▥ Basic Research

**Benoit Labonté, Ph.D.,** Laval University, Canada, will be examining a female-specific gene network to determine how it relates to stress susceptibility in women with depression. Depression symptoms differ in men and women, but the molecular mechanisms behind this difference are unclear. The study will continue Dr. Labonté's work in mice on a

gene called Slit1, which appears to be the hub of this gender-specific gene network. The goals are to investigate Slit1's activity under chronic stress conditions in men and women, to determine whether the combination of stress and depression, mediated through the gene, creates changes in the structure of the brain's medial prefrontal cortex in women as they do in men, and to identify Slit1's impact on stress susceptibility behaviors.

▥ Basic Research

**Jacopo Lamanna, Ph.D.,** San Raffaele Vita-Salute University, Italy, aims to understand how chronic stress may give rise to depression through changes in the transmission of dopamine, by examining changes in the neural circuitry regulating dopamine in the prefrontal cortex and amygdala. This research could shed light on whether these circuits are also the target of the fast-acting antidepressant ketamine. Dr. Lamanna will study changes to the prefrontal cortex circuits generated under different dopamine release and stress conditions in rodent brain slices and also trace changes in the activity of these circuits in stress-vulnerable, stress-resilient and ketamine-treated rats.

▥ Basic Research

**Talia Newcombe Lerner, Ph.D.,** Northwestern University, will explore the neural circuitry that makes some people susceptible to depression and others resilient. The study, conducted in mice, will analyze whether the strength of specific brain connections connected to dopamine transmission can predict depression resilience in individuals, and whether manipulating these connections can give rise to depressive behavior. The goal is also to learn whether gender and early life experiences may interact to control the development of these neural circuits, as women and people who have experienced early life trauma are at higher risk of depression.

▥ Basic Research

**Florian Plattner, Ph.D.,** University of Texas Southwestern Medical Center at Dallas, hopes to learn more about the cAMP/PKA molecular signaling pathway, which aids communication between brain cells and has been implicated in depression. Antidepressant medications that target this pathway can be effective but come with significant side effects, making it important to look for new compounds to target

the pathway. The study will first examine how the pathway is affected by common antidepressants and by acute and chronic stress. The next step will be to test compounds called small-interfering peptides, developed by Dr. Plattner, which target the pathway to determine how the compounds may affect brain cell function and behavior in mice and in brain tissue donated by deceased depression patients

🧬 Basic Research

**Christophe Proulx, Ph.D.,** Laval University, Canada, will build on previous observations suggesting the neurons in the brain's lateral habenula are involved in depression, through their role in the neural reward system to deliver "disappointment" signals. Dr. Proulx will analyze the connection between the lateral habenula and another area of the brain called the dorsal raphe nucleus, which plays a key role in controlling emotion and selecting actions. The goal is to manipulate the connection between these two areas to determine how this may promote depressive behaviors in mice, and to look for dysfunctional information transmission between the two areas in brain slices across different animal models of depression.

🧬 Basic Research

**Francisco Romo-Nava, Ph.D.,** University of Cincinnati, will study the effectiveness of spinal cord stimulation for treating major depressive disorder. Past research has linked depression to an excess of information traveling through the spinal cord to the brain, but the treatment potential of spinal cord stimulation has not yet been explored. Dr. Romo-Nava will test the hypothesis that spinal cord stimulation via electrodes placed on the skin will reduce depression symptoms by acting on the sensory system that gives rise to emotional awareness, and that the technique will be safe to use in adult patients.

🧬 Next-Generation Therapies

**John Patrick Ryan, Ph.D.,** University of Pittsburgh, will investigate the connection between diabetes and depression as it may manifest in the brain. Although each condition is known to exacerbate the symptoms of the other, the neural connections that link them are not known. Dr. Ryan will test whether this interaction is driven by activity in the dorsal anterior cingulate (dACC), a brain region central to executive

control that has shown disrupted connectivity in people with high insulin resistance, and has shown similar irregularities in depression patients.

🧬 Basic Research

**Surjo Raphael Soekadar, M.D.,** University of Tubingen, Germany, hopes to pilot a new brain stimulation technique for treating depression. Dr. Soekadar proposes an approach that, instead of giving static stimulation to the brain as existing technology does, responds to fluctuating brain activity in real time. His team will combine a brain-computer interface with transcranial electric brain stimulation to regulate ongoing changes in frontal lobe activity, which is compromised in depression in ways that impair memory, attention, and other functions. They will then test the efficacy of this technology in people with depression.

🧬 Next-Generation Therapies

**Jonathan P. Stange, Ph.D.,** University of Illinois at Chicago, seeks to identify biomarkers for problematic responses to sadness found in major depressive disorder. He will focus on brain networks implicated in disrupted emotion regulation linked to depression, alongside the body's parasympathetic response, the part of the nervous system that conserves energy. He expects to find increased activity in emotion processing circuits and decreased activity in cognitive control circuits that, together, correspond with impaired emotion regulation, as shown by a weak parasympathetic response and difficulty recovering from sadness.

🧬 Diagnostic Tools/Early Intervention

**Hanna Maria van Loo, M.D., Ph.D.,** University of Groningen, Netherlands, aims to identify genetic risk factors in major depression. Taking advantage of the existing Biobank LifeLines study, which offers access to genome-wide date for about 70,000 Dutch patients, along with information about lifestyle, environment, and other diseases, Dr. van Loo will use state-of-the-art statistical methods to find genetic traits and environmental factors that present risks for depression.

🧬 Diagnostic Tools/Early Intervention

**Crystal Vergara-Lopez, Ph.D.,** The Miriam Hospital, Brown University, will study stress as a risk factor for adolescent depression. The work will focus on the changes in neural circuitry, including neuroendocrine function, that occur as a person copes with stress. Dr. Vergara-Lopez is working toward identifying relevant biomarkers that will aid in the diagnosis and treatment of adolescents with depression.

Basic Research

**Veronika Vilgis, Ph.D.,** University of California, Davis, will study how early childhood stress can lead to depression in adolescent girls. The work will draw from a large study of girls, ages 9-18, to examine how they react to mother-daughter conflict, and if this can be used as a predictor for depression during adolescence. Dr. Vilgis hopes the study seeks to uncover the neurobiology underlying adolescent depression to facilitate the development and selection of effective treatment approaches.

Basic Research

# EATING DISORDER

**Jason Matthew Lavender, Ph.D.,** University of California, San Diego, is working to better understand anorexia nervosa, a disorder that predominantly affects girls and women. He hopes to clarify how the disorder may be related to altered brain functioning, using fMRI to study the brains of adult women with and without the disorder while they complete a task requiring mental flexibility, an ability often limited in those with anorexia nervosa. These neuroimaging data will be combined with data collected from the women via smartphone, gathering information on their real-time emotions and thoughts, to examine the relationship between brain functioning and daily functioning in those with anorexia nervosa.

Basic Research

# MENTAL ILLNESS GENERAL

**Megan Crow, Ph.D.,** Cold Spring Harbor Laboratory, will survey patterns of gene expression to gain a better understanding of the diverse array of cells in the brain. The project will characterize gene expression patterns in both mouse and human nervous systems and use this information to identify networks that or unique to and shared across species. Dr. Crow plans to focus on defining the specific cell types and networks in which psychiatric disease genes play a role. (cell types in the brain)

Basic Research

**Steven Willem Flavell, Ph.D.,** Massachusetts Institute of Technology, is interested in untangling the complexity and flexibility of the serotonergic system, the most common target of psychiatric drugs. Working in the worm C. elegans, which shares some genes and brain circuits with mammals, he will monitor the response of brain circuits in the sertonergic system to serotonin. By manipulating the genes involved in this system and observing the responses in specific brain circuits, Dr. Flavell hopes to shed light on the specific mechanisms of this critical system. (serotonin)

Basic Research

**Julijana Gjorgjieva, Ph.D.**, Max-Planck Institute of Brain Research, Germany, aims to characterize specific aspects of normal brain development. The work will focus on spontaneous activity, a phenomenon observed in the brain prior to a sensory experience and may have a role in shaping brain-wide circuits. By imaging and recording the activity of cells in the brains of young mice, Dr. Gjorgjieva hopes to tease apart the relative influences of various perturbations of spontaneous activity. (brain development)

Basic Research

**Elizabeth J. Glover, Ph.D.,** Medical University of South Carolina, seeks a better understanding of how a brain region called the lateral habenula (LHb) regulates the release of dopamine, a molecule that signals reward in the brain. The LHb is thought to mediate aversive responses, such as avoidance, and therefore has implications for a number of neuropsychiatic disorders. Using approaches including high-resolution microscopy and optogenetics, Dr. Glover hopes to illuminate the LHb's role in regulating the balance between reward and aversion. (dopamine)

Basic Research

**Adam John Harrington, Ph.D.,** Medical University of South Carolina, seeks a better understanding of how alterations in the balance of excitatory and inhibitory signals in the brain may give rise to neuropsychiatric disorders. The project will focus on the role of a gene known as PCDH17, which has been implicated in major mood disorders and schizophrenia. By manipulating the expression of PCDH17 in key regions in the brains of mice, Dr. Harrington hopes to provide new insights into the gene's role in excitatory-inhibitory balance. (excitation/inhibition circuitry)

Basic Research

**Koichi Hashikawa, Ph.D.,** New York University School of Medicine, aims to elucidate how winning experiences strengthen brain circuitry underlying aggression, a trait widely observed in a variety psychiatric disorders including PTSD and schizophrenia. The team will train mice to act more aggressively through winning experiences, and monitor the levels at which various genes are expressed in the brain over the course of this training. Dr. Hashikawa will focus on a brain region called the ventromedial hypothalamus ventrolateral area, which has been implicated in aggressive behavior in mice. (aggression circuitry)

Basic Research

**Bryan M. Hooks, Ph.D.,** University of Pittsburgh, will study the connections between interneurons—the inhibitory nerve cells that modulate neural circuits between sensory and motor neurons and the central nervous system—to create a map of fundamental interneuron "wiring" in the frontal cortex. The goal is to determine whether different neural inputs to the frontal cortex target different interneurons involved in inhibiting neural activity. Changes to this inhibitory circuitry in the frontal cortex have been linked to schizophrenia, among other mental illnesses. Dr. Hooks will develop a rat model of interneuron connections that can test whether the individual circuits involving each interneuron can be selectively silenced, to promote specific choices in decision-making or behavior. (inhibition circuitry)

Basic Research

**Elizabeth Diana Kirby, Ph.D.,** Ohio State University, is exploring the spread of the brain's secreted proteins, which may have far-reaching impacts on brain function and are implicated in multiple disorders from anxiety to stroke. Dr. Kirby will be using genetic tools to label all the proteins in hippocampal neural stem cells with chemical tags within brain slices. Her team will use these tags to identify and visualize some of the proteins after they are released from their original cells. The goal is answer essential questions about where secreted proteins travel within the brain and how long they take to get their destinations, which could illuminate their roles in disease. (brain proteins)

Basic Research

**Lee Lovejoy, M.D., Ph.D.,** Columbia University, will be studying the neural circuitry behind executive function, the suite of cognitive processes that includes memory, focus and attention. Impaired executive function can be disabling in several psychiatric illnesses, including depression and ADHD, and treatments to improve executive function are critically lacking. Dr. Lovejoy's research seeks to clarify how neurons in the brain's prefrontal cortex, the amygdala and other regions contribute to executive function. The study will record brain activity from hundreds of neurons in monkeys trained on a complex cognitive task, as well as chemically alter neurons so that they can be selectively inactivated to determine how their action relates to executive function. (executive function)

Basic Research

**Mikael Lars Lundqvist, Ph.D.,** Massachusetts Institute of Technology, will continue to explore the macro- and microcircuitry in the brain that supports working memory, a cognitive function that can be impaired across a number of mental illnesses including schizophrenia. The study will build on insights that the neural activity supporting working memory does not result from sustained spiking of neural activity, but rather is contained in bursts of transient neural activity at different interacting brain wavelengths. The pattern may allow multiple thoughts to be held simultaneously in working memory. This type of dynamic processing, often hidden by research that averages neural activity across multiple experiments, may underlie many cognitive functions. (working memory)

IDG Basic Research

**Thomas Hatton McCoy, M.D.,** Massachusetts General Hospital/Harvard University, will study new ways to identify the signs and symptoms of psychiatric disability that appear in electronic medical records, and to use machine learning to organize those markers into useful summary scores of disability. The hope is to find new ways of understanding the biology that underlies conditions such as bipolar disorder or schizophrenia. The research will use clinical documentation from tens of thousands of patients who have donated their health records and genetic material to research. (data mining medical records)

IDG Diagnostic Tools/Early Intervention

**Francesca Maria Pia Notarangelo, Ph.D.,** University of Maryland, Baltimore, wants to learn more about the influence of gut microbes on cognition, using antibiotic-treated rats. Preliminary studies show that the intestinal microbiota regulates a metabolic pathway that produces several compounds that impact the brain, including kynurenic acid. Elevated brain levels of this compound have been linked to cognitive impairment in animal studies. The research will examine the relationship between microbiota, the metabolic pathway and cognitive ability in rats. The study's findings could help researchers learn more about the exact molecular mechanisms at work linking gut microbes and cognitive function, which can be impaired in people with Schizophrenia and other psychiatric disorders. (microbiome and cognition)

IDG Basic Research

**Marco Onorati, Ph.D.,** University of Pisa, Italy, will examine how a host of congenital infections, including the Zika virus, may lead to microcephaly. The condition affects the development of the brain's cortical cells, leading to developmental delay and intellectual disability. The study will focus on how Zika and TORCH (Toxoplasma, Other, Rubella, Cytomegalovirus and Herpes simplex virus) congenital infections disrupt cortical development, by observing their effect on NES, a type of self-renewing neural stem cells that serve as a unique lab model for early human brain development. Dr. Onorati wants to know how these infections impact NES cell division and death and their ability to produce viable, functioning neurons. The study will also shed light on the processes underlying normal human brain development. (viral infection of the brain)

IDG Basic Research

**Martin Schain, Ph.D.,** Columbia University, hopes to improve the positron emission tomography imaging technique to study the role of inflammation in schizophrenia and major depression. While PET imaging can pick up on neuroinflammation, it has not yet become sensitive enough to produce consistent results. Dr. Schain will test a new PET approach that should be able to track more data throughout the brain and avoid blood samples, which are tough to analyze. His team will use this novel method to measure neuroinflammation levels in people with schizophrenia and depression, as compared to people with neither condition. (inflammation imaging)

IDG New Technologies

**Elliot H. Smith, Ph.D.,** Columbia University, will investigate the activity of neurons in two brain regions linked to many psychiatric disorders: the amygdala, the brain's fear center, and prefrontal cortex, key for higher level processing. Dr. Smith will measure activity patterns in these two regions among people watching film clips, who will later describe the content and emotions of the scenes. He hopes to uncover how these neurons track social decision-making, laying the groundwork to treat social symptoms of different illnesses. (fear, social symptoms)

IDG Basic Research

**Ryan T. Strachan, Ph.D.,** University of North Carolina at Chapel Hill, will develop a new way of identifying highly specific drugs for neuropsychiatric illness. Dr. Strachan will focus on a class of proteins, known as G protein-coupled receptors, screening them for sensitivity to a host of chemicals. The work should identify highly specific chemical tools that will allow researchers to not only understand complex cellular pathways, but also devise new treatment strategies for a range of disorders. (drug development)

IDII Next-Generation Therapies

**Rodrigo Suarez, Ph.D.,** University of Queensland, Australia, will examine how the cortex, the region of the brain responsible for thought, memory, and consciousness, develops at its earliest stages. Using a marsupial model, Dr. Suarez will explore the wiring of neural circuits in the cortex during fetal development. The work will reveal how neural connections change in health and disease, informing the development of novel strategies for the diagnosis and treatment of mental illness. (cortical development)

IDII Basic Research

**Elsa Suberbielle, D.V.M, Ph.D.,** INSERM, France, will study how inflammation in the brain leads to mental illness and neurodegenerative disease. Dr. Suberbielle recently found that breaks across both strands of the DNA double helix play a central role in neural function and cognition. The new studies will explore how these DNA breaks impact disease progression, offering insights that may prove useful in the development of novel therapeutics to treat a wide range of neurological disorders. (inflammation)

IDII Basic Research

**Cinzia Vicidomini, Ph.D.,** Massachusetts General Hospital, Harvard University, will study how changes in neural shape during development contribute to learning, social memory and emotional reactions. Neurons communicate using dendritic spines, finger-like projections protruding from the surface of the cell. During development – and in some diseases – the number of spines fluctuates, altering neural connections. Dr. Vicidomini will use novel genetic and viral systems to study how these changes in neural connectivity affects the function of specific neural circuits in the brain. (dendritic spines)

IDII Basic Research

**Karen L. Fortuna, Ph.D., MSW,** Dartmouth Medical School, Dartmouth College, will test a novel method to treat mental illness and chronic medical disease among middle-aged and older adults. People with serious mental illness are disproportionately affected by chronic health conditions. Dr. Whiteman has developed a new "PeerTECH" system that combines technology - in the form of a smartphone application – with peer care to alleviate the symptoms of mental illness while improving overall health. (treating comorbidity)

IDII Next-Generation Therapies

**Andrea Young, Ph.D.,** Johns Hopkins University, will examine whether or how the use of mental health services among children impacts the risk of substance abuse later in life. The work, which will focus on children with mania, is built upon previous studies, which suggest that mental health services might reduce the risk of substance abuse in adolescents. Dr. Young hopes to develop a structured and well-defined mental health strategy for children that will reduce both psychiatric episodes and substance use while improving access to quality care. (impact of mental health services)

IDII Diagnostic Tools/Early Intervention

# MULTIPLE DISORDERS

**Brent William Asrican, Ph.D.,** University of North Carolina at Chapel Hill, will investigate a particular type of brain cell that may play a role in both autism spectrum disorders and schizophrenia. These cells are known as cholecystokinin (CCK)-type inhibitory neurons. In studies of lab animals, Dr. Asrican will test a novel mechanism through which the CCK neurons may regulate activity in a brain region known as the hippocampus. (hippocampal regulation; autism spectrum disorder, schizophrenia)

IDII Basic Research

**Steve Davidson, Ph.D.,** University of Cincinnati, will illuminate the role of particular brain cells called mGluR2 neurons in pain tolerance and psychiatric disorders linked with chronic pain, which include major depressive disorder and anxiety disorders. Using mice, the team will manipulate the activity of mGluR2 neurons in an area known as the "emotional brain," the anterior cingulate cortex. Dr. Davidson predicts that these changes in the brain will alter pain tolerance and depression-like behaviors. (pain tolerance; depression, anxiety)

Basic Research

**Annegret Lea Falkner, Ph.D.,** New York University, will probe brain circuitry linked to aggressive behaviors, which are characteristic of psychiatric disorders ranging from schizophrenia to attention deficit hyperactivity disorder (ADHD). Working in lab animals, Dr. Falkner will use a combination of optical tools to study a brain region called the ventromedial hypothalamus, ventrolateral area (VMHvl) thought to regulate aggressive behavior. This project aims to offer insight into how aggressive behaviors may arise as a result of regulatory failure in the VHMvl. (aggression; schizophrenia, ADHD)

Basic Research

**Vincenzo Alessandro Gennarino, Ph.D.,** Baylor College of Medicine, seeks to characterize effects in the brain when a protein called PUM1 is missing. This protein regulates the expression of genes thought to be involved in neurodegenerative diseases including spinocerebellar ataxia, Alzheimer's disease, and Parkinson's disease. Dr. Gennarino will study how loss of PUM1 affects patient derived-cells, and idetify the full repertoire of genes that PUM1 regulates in the mouse brain. (gene regulation; Parkinson's, Alzheimer's)

Basic Research

**Laura Germine, Ph.D.,** McLean Hospital/Harvard University, aims to determine whether people with elevated depression and anxiety symptoms perform more variably on cognitive tests. Her approach will show how the experience of negative affect-related symptoms, such as those of depression and anxiety, are related to common stressors and cognitive performance in everyday life. Dr. Germine hopes that these results will provide insights into how variations in negative affect are linked to differences in how the brain processes information. (cognition; depression, anxiety)

Basic Research

**Olivier Gschwend, Ph.D.,** New York University, is interested in the interactions between two brain regions, the prefrontal cortex and mediodorsal thalamus, which tend to be perturbed in patients with schizophrenia and autism. Dr. Gschwend will focus on the roles of NMDA and mGluR5 receptors, both structures involved in signaling between brain cells, in the interactions between these two brain regions. (signaling; schizophrenia, autism spectrum disorder)

Basic Research

**Sarah M. Haigh, Ph.D.,** University of Pittsburgh, will investigate the relationship between the abnormal processing of sounds and impaired ability to distinguish emotions seen in both autism and schizophrenia. The team will compare the performance of adults with autism or schizophrenia with that of healthy adults on tests of the ability to discriminate the pitch and emotional meaning of sounds. (auditory processing; schizophrenia, autism spectrum disorder)

Basic Research

**Keren Haroush, Ph.D.,** Stanford University, seeks insights into the processes that underlie social interactions, which are impaired in disorders such as schizophrenia and autism, at the level of a single brain cell's activity. Through studies of non-human primates, the team will study social interactions and how they are influenced by deep brain stimulation, a technique that is already used to treat certain brain disorders. (social interaction; schizophrenia, autism spectrum disorder)

Basic Research

**Matthew Carl Hearing, Ph.D.,** Marquette University, will take a closer look at the idea that stress-induced dysfunction n the medial prefrontal cortex can disrupt cognitive function. Repeated exposure to stress is thought to be a risk factor for mental illnesses including depression, schizophrenia and PTSD, each of which may include cognitive dysfunction as

a symptom. Dr. Hearing will use a variety of techniques to determine if molecular signaling through a neuron channel called GIRK is important for cognitive function, and whether alterations in GIRK signaling play a significant role in cognitive dysfunction related to chronic stress. The study will also test whether a compound that targets GIRK channels may have a therapeutic effect in treating cognitive dysfunction. (stress and cognition; depression, schizophrenia, PTSD)

⬭⬭ Basic Research

**Sarah Rachel Heilbronner, Ph.D.,** University of Rochester, hopes to learn more about a part of the brain called the posteromedial cortex, which may harbor abnormalities in patients with depression and schizophrenia. Despite this role, little is known about this difficult-to-research brain region. The study's goal is to characterize the posteromedial cortex's connections with two other parts of the brain affected by psychiatric disorders—the striatum and the prefrontal cortex. Dr. Heilbronner would like to know if there are specific "hubs" of information integration between these brain regions that might be especially vulnerable to disruption in depression and schizophrenia. (circuitry; depression, schizophrenia)

⬭⬭ Basic Research

**Laura Marianne Huckins, Ph.D.,** Icahn School of Medicine at Mount Sinai, will analyze gene expression in the world's largest dataset of bipolar disorder and schizophrenia cases. Dr. Huckins will use powerful machine-learning techniques to characterize the similarities and differences between the two conditions in order to better understand each's pathology. She hopes this work will provide insight into the genetic and molecular mechanisms underlying disease risk in bipolar disorder and schizophrenia. (genetics; bipolar disorder, schizophrenia)

⬭⬭ Basic Research

**Soonjo Hwang, M.D.,** University of Nebraska Medical Center, will conduct a randomized, double-blind, placebo-controlled trial of the effects of oxytocin on adolescents with various psychiatric issues: ADHD, oppositional defiant disorder (ODD), conduct disorder (CD), or disruptive mood dysregulation disorder (DMDD). Using fMRI and magnetoencephalography , Dr. Hwang will look at activity in the amygdala and other areas associated with emotional

regulation while participants perform different tasks. This data will be correlated to any symptom improvement to gauge oxytocin's therapeutic potential. (drug trial; ADHD, adolescent mood disorders)

⬭⬭ Next-Generation Therapies

**Luke Williamson Hyde, Ph.D.,** University of Michigan, will use neuroimaging in adolescent twin populations to relate differences in brain function to antisocial behavior (AB), a predictor of psychiatric disorders in adulthood. He will examine the relationship between increased AB in adolescence and brain activity in the amygdala in response to threats, the ventral striatum in response to rewards, and the prefrontal cortex during an inhibitory control task. He will also look at the impact of environmental factors like harsh parenting and exposure to violence on AB and brain function. He will assess the extent to which differences in brain function and AB are environmental versus genetic in causation. (antisocial behavior, mood disorders)

⬭⬭ Basic Research

**Emily G. Jacobs, Ph.D.,** University of California, Santa Barbara, notes that sex hormones can alter the brain's dopamine system, whose dysfunction is observed in Parkinson's disease, attention deficit hyperactivity disorder, and drug addiction. Combining methods from brain imaging, endocrinology, and genetics, Dr. Jacobs will study how concentrations of different hormones impact dopamine production and release in the brain. This work will expand knowledge on sex differences in dopamine neurotransmission and may provide insights into how hormones impact risk for numerous conditions. (ADHD, Addiction, Parkinson's)

⬭⬭ Basic Research

**Sun-Hong Kim, Ph.D.,** Johns Hopkins University, is taking a closer look at how the anterior insula participates in social cognition, which can be impaired across multiple mental illnesses such schizophrenia, ASD and bipolar disorder. Dr. Kim will be examining circuitry connecting the anterior insula and a brain region called the dorsal raphe nucleus. The study will focus on how this circuit may contribute to recognition of novel social input, and will provide more information about how the serotonin system contributes to novelty recognition within the anterior insula. (social cognition; autism spectrum disorder, schizophrenia, bipolar disorder)

⬭⬭ Basic Research

**Emma Eileen Mary Knowles, Ph.D.,** Yale University, will use magnetic resonance spectroscopy to measure levels of compounds related to phospholipids in the brains of healthy people and those with depression and bipolar disorder, as a first step to determining whether phospholipids may be useful biomarkers for diagnosing and treating mental illnesses. Phospholipids can be measured in blood samples, but it is unclear how their blood levels relate to levels in the brain. (biomarkers; depression, bipolar disorder)

Diagnostic Tools/Early Intervention

**David R. Kopala-Sibley, Ph.D.,** Stony Brook University School of Medicine, seeks to identify links between parenting behaviors, neural development and the development of depression and anxiety symptoms. The study will include a group of three-year old children and parents followed for more than 10 years, and a second group of adolescent girls. The goal is to use fMRI to examine neural markers of the Default Mode Network and amydala-prefrontal connectivity to determine whether they can be used to predict the development of depression and anxiety over time in the children. (biomarkers; depression, anxiety)

Diagnostic Tools/Early Intervention

**Romain Ligneul, Ph.D.,** Fundação Champalimaud, Portugal, will use updated techniques to precisely measure serotonin activity in nerve cells in mice, to resolve previous discrepancies in how levels of this neurotransmitter—an important target in treating depression, anxiety and other mental illnesses-- have been determined. The hypothesis is that serotonin-driven neural activity does not correspond linearly with serotonin release and activation of serotonin receptors. Dr. Ligneul will induce and track serotonin activity in several behavioral experiments, and analyze how doses of antidepressant drugs may affect the relationship between serotonin neural activity and serotonin release. (serotonin; depression, anxiety)

Basic Research

**Qing-song Liu, Ph.D.,** National Institutes of Health, will study the function of a gene called CYFIP1 on human chromosome 15, which has been associated with increased susceptibility to developmental and motor delay, schizophrenia, psychosis and ASD. The study seeks to understand how vari-

ations in the dosage of the gene may affect neural circuits in brain regions relevant to schizophrenia and other illnesses. Among the goals are to determine how CYFIP1 deletion affects circuit function in the frontal cortex and how this altered function might correspond to behavioral changes in mice. (genetics; schizophrenia, psychosis, autism spectrum disorder)

Basic Research

**Cristina Marquez, Ph.D.,** Instituto de Neurociencias de Alicante, Universidad Miguel Hernandez, Spain, hopes to learn more about the neural circuitry behind social relationships, which can be dysfunctional across a number of mental illnesses including ASD, anxiety disorders and depression. The study will focus on how rats process social reward cues during a "partnership" task, with special attention paid to the activity of neurons in the brain's anterior cingulate cortex (ACC) during the social task. The goal is to use optogenetic and other tools to monitor and manipulate neural activity in this region, to identify how the ACC in rodents processes social cues received from other animals and integrates this information to produce a specific behavior. (social circuitry; autism spectrum disorder, anxiety, depression)

Basic Research

**Natalie Matosin, Ph.D.,** Max-Planck Institute of Psychiatry, Germany, will examine whether overexpression of the FKBP5 gene may create a distinct pattern of gene expression in the brain and body that could be used to identify psychiatric patients who would benefit from drugs that suppress the gene's activity. FKBP5 is a key regulator of the stress response. Previous research by Dr. Matosin's lab indicates that overexpression of the gene is linked to long-term changes in cellular and systemic stress levels that may increase the risk of psychiatric illnesses such as depression, bipolar disorder and schizophrenia. (genetics; depression, bipolar disorder, schizophrenia)

Basic Research

**Christian Meisel, M.D.,Ph.D.,** National Institute of Mental Health, will explore the role of phase transitions in mental illness, and whether an phenomenon known as critical slowing down can be used as a biomarker of disease susceptibility in chronic disorders such as schizophrenia and

epilepsy in which there is often a sudden phase transition between health and disease, such as psychotic break--or an epileptic seizure. The precursor to the transition, critical slowing down, occurs when a stable system weakens before the onset of the phase change. Dr. Meisel will characterize critical slowing down in epilepsy patients with large-scale EEG recordings, and in a rodent model of systemic inflammatory disease using biosensor data. The goal is to provide a method for forecasting recurrent episodes such as seizures and adjusting therapies to match these transitions. (behavior; schizophrenia, pschosis, epilepsy)

🧬 Diagnostic Tools/Early Intervention

**Juan Mena-Segovia, M.D.,Ph.D.,** Rutgers University, will conduct experiments to determine how two parts of the brain contribute to cognitive rigidity, a condition connected to many types of poor mental health. Cognitive rigidity prevents individuals from adapting the execution of an action to meet changes in their environment. Low levels of the neuromodulator acetylcholine have been linked to rigidity, most notably in ASD and Tourette's syndrome. The study will shed light on the relative contributions of two populations of neurons underlying acetylcholine transmission in the brain, which appear to operate in different behavioral contexts, to discover how they may relate to rigidity. (cognitive rigidity; autism spectrum disorder, Tourette's)

🧬 Basic Research

**Nathan Okerlund, Ph.D.,** University of Utah, will explore the role that the cell recycling pathway called autophagy might play in disorders from ASD to Alzheimer's and Parkinson's. Autophagy may recycle unwanted neural synapses—the communicating connections between neurons. Autophagy failures could prevent the brain from "pruning" these connections during normal brain development—a phenomenon that may be responsible for some cases of autism. Dr. Okerland will create mice that incorporate molecular tools he has developed to alter synapse autophagy, to determine whether increased or decreased autophagy can lead to autism-related defects in the mice. If restoring autophagy improves these defects in mice, the cellular recycling pathway could become a therapeutic target. (brain development; autism spectrum disorder, Alzheimer's, Parkinson's)

🧬 Basic Research

**Carlos J. A. B. Pantoja, M.D.,Ph.D.,** Max Planck Institute of Neurobiology, Germany, will use experiments in zebrafish to determine the basis for individual variation in the acoustic startle response. This important defensive behavior occurs in humans as well, and changes in the response have been associated with anxiety disorders and schizophrenia. The study will use whole brain functional imaging to identify the neural circuits involved in individual startle response, including the activity of specific neurons that might affect multiple behaviors at once, and will examine the specific genetics of individual differences in the behavior. (startle response; anxiety, schizophrenia)

🧬 Basic Research

**Kristen Elizabeth Pleil, Ph.D.,** Weill Cornell Medical College, hopes to investigate a neural "switch" that may occur in people with disorders such as schizophrenia, depression, bipolar disorder and PTSD that may make them more likely to abuse alcohol. Many of these individuals report using alcohol to medicate their symptoms. Using a variety of techniques, the study will probe the connections between three parts of the brain involved in alcohol abuse. In particular, Dr. Pleil will study whether a connection between two of the brain regions that is rewarding in healthy individuals drinking alcohol may be weakened in individuals who experience the lack of pleasure and affect associated with many mental illnesses. A second circuit may instead be strengthened in these patients, resulting in drinking to seek relief from negative symptoms. (addiction circuitry; schizophrenia, depression, bipolar disorder, PTSD)

🧬 Basic Research

**Giovanni Provenzano, Ph.D.,** University of Trento, Italy, will test the hypothesis that abnormalities in how some genes are transcribed (the first step of gene expression) during postnatal brain development can contribute to disorders such as schizophrenia and ASD. The study will test this idea in three mouse models, at different stages of development, that mimic some of the symptoms of ASD, Fragile X syndrome and schizophrenia. Dr. Provenzano will then compare any affected gene networks containing transcriptional abnormalities with drug data to uncover any new therapeutic strategies for treating specific symptoms within these illnesses. (genetics; schizophrenia, autism spectrum disorder; Fragile-X)

🧬 Basic Research

**Candace Marie Raio, Ph.D.,** New York University, will examine the effects of stress on strategies for self-control, which is disrupted in depression, anxiety, and different forms of addiction. Part of effective self-control is minimizing that behavior, when it will demand mental effort that could be put to better use elsewhere. Dr. Raio expects to find that people under stress regulate their self-control levels less effectively by picking strategies that require too much of that behavior in the long term, taxing their cognitive resources. She will also investigate how stress impacts the interaction between different brain networks involved in decision-making. (stress; depression, anxiety, addiction)

🧬 Basic Research

**Patrick Eldredge Rothwell, Ph.D.,** University of Minnesota, aims to lay the groundwork for a new treatment targeting autism spectrum disorders and schizophrenia. The gene neuroligin-3—which encodes a protein that bridges the gaps between neurons—has shown mutations among patients with autism and schizophrenia. Using optogenetics, a technique that stimulates brain cells with light, Dr. Rothwell hopes to identify the specific synapses affected in mice lacking neuroglin-3. He will also test whether stimulating affected synapses with light can correct their activity, as a remedy for abnormal synaptic communication. (synaptic communication; autism spectrum disorder, schizophrenia)

🧬 Next-Generation Therapies

**Atsushi Saito, M.D., Ph.D.,** Johns Hopkins University, will examine epigenetic mechanisms that may be disrupted in development and so give rise to intellectual disability, autism, schizophrenia, and mood disorders. Proper development of neuronal connectivity requires changes to the support structure for DNA that, in turn, controls gene expression. Dr. Saito will study a key support protein, SETDB1, that recruits other proteins for brain development, in a process that has been linked to intellectual development. His team hopes to uncover how disruptions to SETDB1 change the connections between neurons and as a result lead to cognitive deficiencies. (epigenetics; autism spectrum disorder, schizophrenia, depression, anxiety)

🧬 Basic Research

**Cody A. Siciliano, Ph.D.,** Massachusetts Institute of Technology, hopes to identify the neural underpinnings of associative learning, a process that is disrupted in illnesses including eating disorders and addiction. Associative learning is the process by which we learn to connect specific behaviors to specific outcomes, and it has been linked to the lateral hypothalamus in the brain. Dr. Siciliano will test the hypothesis that these learning-related projections to lateral hypothalamus respond to internal motivations and drive behavior. (learning; eating disorders, addiction)

🧬 Basic Research

**Tanya Sippy, M.D.,Ph.D.,** New York University, will study a brain region called the striatum thought to play a role in reward processing, which is abnormal in many psychiatric conditions such as depression, addiction, and obsessive compulsive disorder. Looking at mice, Dr. Sippy will test how neurons in the striatum respond to different types of reward. Her team will also look at whether striatal neurons track discrepancies between expected and received reward, as well as the role of the neurotransmitter dopamine in communicating between these cells. (reward processing; depression, addiction, OCD)

🧬 Basic Research

**Katharine Rachel Smith, Ph.D.,** University of Colorado, Denver, will study the mechanisms behind overly responsive neurons, whose high activity in brain regions key for learning and memory contributes to autism, schizophrenia, and other psychiatric disorders. Dr. Smith's team will examine proteins that have been genetically linked to psychiatric illness, and how the activity of these proteins changes communication between neurons. She hopes this work will uncover new targets for treating psychiatric symptoms that stem from hyperactive neurons. (learning and memory; autism spectrum disorder, schizophrenia)

🧬 Basic Research

**Marta Elaine Soden, Ph.D.,** University of Washington, aims to develop a system for evaluating genetic susceptibility to stress-related psychiatric illness. To build this system, she will look at the gene encoding receptors for a hormone released by stress, called corticotropin-releasing factor, which acts on a brain region linked to psychiatric disorders. Her team will track the interactions between CRF receptors and ways these interactions might mediate behavior. She hopes her findings will shed light on specific gene-environment interactions that give rise to psychiatric illness via stress responses. (stress hormones; depression, anxiety, PTSD)

🧬 Basic Research

**James Fitzhugh Sturgill, Ph.D.,** Cold Spring Harbor Laboratory, will examine the complex genetic and environmental interactions that converge to cause attention deficit, the hallmark of many brain disorders. The work will focus on the dynamics of two types of chemical messengers, cholinergic and dopaminergic signals, in response to unique environmental cues. Correlating these signals with reaction times will offer insight into how these messengers contribute to diseases like ADHD and schizophrenia. (attention; ADHD, schizophrenia)

🧬 Basic Research

**Zhibing Tan, M.D., Ph.D.,** Augusta VA Medical Center, Georgia Health Sciences University, will explore the neural circuits that control attention. Attention deficits are a hallmark of many mental disorders, including schizophrenia, ADHD, and Alzheimer's disease. Dr. Tan will study the neural connections between two regions of the brain, the ventral hippocampus and the medial prefrontal cortex, to gain new insight into the mechanisms underlying attention deficits. (attention; schizophrenia, ADHD, Alzheimer's)

🧬 Basic Research

**Jerome H. Taylor, M.D.,** Yale University, will explore the use of melatonin to treat people who are at high risk of developing schizophrenia. The work will target adolescents and young adults who exhibit mild symptoms of psychosis, which puts them at risk of developing schizophrenia within six months. Melatonin is low in patients with schizophrenia

and it has been suggested that the supplement might protect neurological function. Dr. Taylor will determine if melatonin plays a protective role in these high risk adolescents. (melatonin supplements; psychosis, schizophrenia)

🧬 Next-Generation Therapies

**Jillian Lee Wiggins, Ph.D.,** San Diego State University, is working to identify children at high risk of developing irritability and, therefore, need a doctor's help. Irritability is more than just a phase; it is a major risk factor for multiple mental disorders, including depression, bipolar disorder, and ADHD. Dr. Wiggins will follow children who are at high risk of developing irritability because their mothers are depressed. The work will correlate brain imaging and measures of irritability in an effort to better identify and treat children with irritability. (imaging; depression, bipolar disorder, ADHD)

🧬 Diagnostic Tools/Early Intervention

**Ralf Dieter Wimmer, Ph.D.,** New York University, will examine the neural connections and circuitry that control attention. Attention deficits are a major symptom in many neurodevelopmental disorders, including ADHD, schizophrenia, and autism spectrum disorders. Dr. Wimmer's work will focus on understanding the top level neural networks in a region of the brain called the mediodorsal thalamus that play a key role in controlling attention. (attention; ADHD, schizophrenia, autism spectrum disorder)

🧬 Basic Research

**Susan K. Wood, Ph.D.,** University of South Carolina, will work to understand why women are more than twice as likely to suffer from stress-related mental disorders, like major depression, than men. Estrogen appears to drive these differences, and Dr. Wood has identified the HMGB-1 gene as a key mediator of estrogen's effects. The work aims to determine the genes that are controlled by HMGB-1 in an effort to understand the molecular mechanisms that make women more susceptible to stress-related disorders. (stress and gender; depression, anxiety)

🧬 Basic Research

# OCD
*Obsessive-Compulsive Disorder*

**Thomas V. Fernandez, M.D.,** Connecticut Mental Health Center, Yale University, strives to achieve a more comprehensive picture of the genetic underpinnings of obsessive-compulsive disorder (OCD). Dr. Fernandez will search for forms of genetic variation that remain to be explored in connection with OCD, such as the duplication or deletion of sections of the genome, known as copy number variation. The team will then integrate the risk genes they find with data on brain regions, developmental time periods, and biological processes whose functions are disrupted in OCD patients.

Basic Research

**Oded Klavir, Ph.D.,** University of Haifa, Israel, will study the role of the midbrain's dopamine system in OCD, which affects the brain's ability to perform automated and goal-directed behaviors. When communication between the two systems underlying these behaviors goes awry, information that is usually processed automatically could be transformed into obsessions, and automated habitual behaviors could evolve into compulsive behaviors. In experiments with mice, Dr. Klavir will test the idea that connections between the circuits that control habit information and goal-directed behavior information, through the midbrain dopamine system, are important to normal and abnormal action control.

Basic Research

# PSYCHOSIS

**Claudia M. Haase, Ph.D.,** Northwestern University, notes that caregivers for youth at ultra-high risk (UHR) for psychosis are themselves at considerable risk for mental and physical health problems. To address this issue, her team will evaluate the negative emotional interactions between UHR youth and their caregivers through measurements of their behavior, experience, physiology, and change in the expression of their genes. Dr. Haase aims to use this information to determine how negative emotions in UHR youth-caregiver relationships predict the caregiver's mental health.

Basic Research

**Manreena Kaur, Ph.D.,** Monash University, Australia, will be studying a new way to target treatments for auditory hallucinations, a feature of schizophrenia that occurs in more than 70 percent of patients. Dr. Kaur is working to improve fMRI imaging to pinpoint brain circuitry involved in these hallucinations on an individual basis, so that a promising non-invasive technology called repetitive transcranial magnetic stimulation (rTMS) can be expanded to treat auditory hallucinations in schizophrenia. The study could also improve the use of rTMS in treating other mental illnesses.

Next-Generation Therapies

**Deepak Kumar Sarpal, M.D.,** University of Pittsburgh, will identify neurological mechanisms underlying recovery from psychosis that results from patients taking antipsychotic medication. His team will look at how 12 weeks of antipsychotic use affects symptoms in relation to brain activity, as measured by magnetic resonance imaging. They predict that successful treatment will be linked to changes in the medial prefrontal cortex, a key brain region for executive function. Dr. Kumar hopes this research will point toward new neurobiological targets for treating psychotic disorders.

Basic Research

**Gisela Sugranyes, M.D., Ph.D.,** Institut D'investigacions Biomèdiques August Pi I Sunyer, Spain, will study the schizophrenia-like disorder NMDAR encephalitis. Dr. Sugarnyes is most interested in the role of so-called "glutamatergic metabolites," chemical messengers that control neural function and connectivity in the brain. The work could offer insight into how the complex symptoms of psychosis arise.

Basic Research

**Lauri Tuominen, M.D., Ph.D.,** Massachusetts General Hospital, Harvard University, will investigate the role of dopamine in the development of disorders featuring psychosis, such as schizophrenia. The work will test if hyperactive dopamine causes patients to have inappropriate emotional

responses, and determine if this reaction leads to psychotic symptoms. Dr. Tuominen's goal is to advance the basic understanding of mechanisms underlying psychosis, in an effort to improve treatment strategies for schizophrenia and other disorders involving psychosis.

✐ Basic Research

## PTSD
*Post-Tramumatic Stress Disorder*

**Roee Admon, Ph.D.,** University of Haifa, Israel, aims to better understand a brain pathway that may contribute to resiliency and vulnerability to stress, work that has implications for the treatment of post-traumatic stress disorder (PTSD). Dr. Admon's research will bridge the gap between human and lab animal studies by manipulating this pathway through the administration of amisulpride, a drug known to spur the release of the stress-regulating neurotransmitter dopamine. Using functional magnetic resonance imaging he will examine the effects of amisulpride administration on stress-vulnerable individuals' brain activity while completing a learning task after exposure to stress.

✐ Basic Research

**Jennifer R. Fanning, Ph.D.,** University of Chicago, aims to develop a model of the brain activity underlying symptoms such as impulsive and self-destructive behavior in post-traumatic stress disorder (PTSD) patients. Dr. Fanning will use measure brain activity in PTSD patients using functional magnetic resonance imaging and electroencephalography. She hopes that the complementary data from these two approaches will provide new insights into cognitive symptoms of PTSD.

✐ Basic Research

**Damion Grasso, Ph.D.,** University of Connecticut and Hartford Hospital, points out that the effects of trauma exposure can be transmitted across generations to influence psychological development of a child, as cases of maternal post-traumatic stress (PTS) illustrate. Prevalent in low-income and minority populations, maternal PTS may compromise the healthy development of a child's biological stress systems through modifications of particular genes' activity, known as epigenetic changes. Using a whole-genome approach, Dr. Grasso aims to identify epigenetic markers associated with maternal PTS in newborn infants and mothers from an urban prenatal care clinic.

✐ Basic Research

**Benjamin Friedrich Grewe, Ph.D.,** at the Brain Research Institute of the University of Zurich, Switzerland, will study the brain networks involved in the overgeneralization of fear responses, a symptom of conditions such as post-traumatic stress disorder. The team will use sounds to train mice to learn a fear-related association, and then examine their brain activity. Focusing on a region called the amygdala, they will image the animals' brains while performing behaviors to study the activity of different networks involved in fear overgeneralization.

✐ Basic Research

**Katherina Hauner, Ph.D.,** Northwestern University, will test a potential therapy for post-traumatic stress disorder that uses a form of noninvasive brain stimulation called transcranial magnetic stimulation. Dr. Hauner aims to use this technology to target and modify the function of the hippocampus, a brain region with an important role in memory. The team will study the effects of this technique, termed hippocampal-cortical network stimulation, or HCN-Stim, in PTSD patients.

✐ Next-Generation Therapies

**Liat Helpman, Ph.D.,** Tel Aviv Sourasky Medical Center, Tel Aviv University, Israel, will study the impact that estrogen may have on neural alterations in the brain's circuitry in women with PTSD and a history of childhood sexual abuse. Women are twice as likely as men to develop PTSD following trauma and those with a history of sexual abuse may not respond as well to PTSD therapies. Dr. Helpman will study the effects of estrogen on the neural circuitry of the brain's limbic system, which is involved in emotional regulation and response, in a group of women with PTSD and a history of abuse.

✐ Basic Research

**Thu Huynh, Ph.D.,** Weill Cornell Medical College, is interested in the neurobiological mechanisms underlying extinction memory formation, which can be impaired in post-traumatic stress disorder (PTSD). Using advanced imaging methods in mice genetically enhanced to extinguish fearful memories, Dr. Huynh will map out changes in neural circuitry following extinction. Additionally, she will use a new technology to delete newly formed connections between neurons to test whether these connections are, in fact, critical for extinction learning.

▮▮▮ Basic Research

**Jonathan Levy, Ph.D.,** Interdisciplinary Center, Herzliya (IDC), Israel, will examine the impact of living near a combat zone upon the development of PTSD. The study will follow children and mothers living in Israel near the Gaza Strip, who have been exposed to years of war (some of whom have been diagnosed with PTSD) with people living farther from the war zone in central Israel. Dr. Levy will use whole-head magnetoencephalography (MEG) imaging to identify neural signals related to empathy and other behaviors, and correlate these signatures with levels of cortisol and oxytocin hormones.

▮▮▮ Basic Research

**Pia-Kelsey O'Neill, Ph.D.,** Columbia University, will study how stimuli of emotional significance—positive, negative or neutral—are mapped on to specific neurons in the brain's amygdala. The neural circuitry connected to these stimuli are important for understanding why certain stimuli that generate negative emotions are exaggerated to become phobias in people with anxiety, or why previously neutral stimuli come to be associated with negative emotional significance, as in cases of PTSD. The goal is to mark, trace and manipulate neurons in the amygdala that respond to stimuli from different senses and of different emotional content, to show how they may be organized and connected to other neurons to produce emotional behavior.

▮▮▮ Basic Research

**Abha Karki Rajbhandari, Ph.D.,** University of California, Los Angeles, will study circuits in the brain crucial for regulating reactions driven by fear. Excessive fear responses can lead to distress and make people more vulnerable to anxiety-related illnesses such as PTSD. Dr. Rajbhandari has identified two circuits in the amygdala—the brain's fear center—linked to regulating and shutting down the fear response. The aim is to better define these circuits and how they work, ultimately to understand their potential as targets for preventing and treating fear-based disorders like PTSD.

▮▮▮ Basic Research

**Prerana Shrestha, Ph.D.,** New York University, will investigate the molecular and cellular components behind upsetting memories that contribute to post-traumatic stress disorder. Dr. Shrestha's team will study three types of neurons in the amygdala—the brain's fear center—that they hypothesize store long-term associative memories. They will focus on the process by which proteins are encoded in these neurons while fear memories are being consolidated, as a potential target for therapeutic intervention in PTSD.

▮▮▮ Basic research

**Benjamin Suarez-Jimenez, Ph.D.,** Research Foundation for Mental Hygiene, Inc./NYSPI, Columbia University, has developed a virtual reality system to study PTSD. Combing this new technology with traditional imaging techniques, Dr. Suarez-Jimenez hops to identify brain regions involved in distinguishing safe and dangerous environments, offering valuable insight into the development of effective diagnostics and treatments for PTSD.

▮▮▮ New Technologies

**Jennifer Brooke Treweek, Ph.D.,** California Institute of Technology, will study the changes in neural circuitry that contribute to PTSD. For some time, researchers have known that patients with PTSD have elevated levels of a chemical messenger known as corticotrophin releasing factor. Dr. Treweek will investigate how this molecule causes changes in the neural circuitry in the brain, providing insight into the mechanisms that make people susceptible to PTSD.

▮▮▮ Basic Research

# SCHIZOPHRENIA

**Tracy Ann Barbour, M.D.,** Massachusetts General Hospital, seeks to better understand the connection between schizophrenia and social anhedonia, the diminished experience of pleasure from social interactions. Dr. Barbour will focus on the relationship between social anhedonia and the way patients process social rewards. By studying the behavior and brain activity of schizophrenia patients and healthy subjects, Dr. Barbour hopes to provide new insights into whether the brain circuits that process social pleasure are distinct from other circuit types.

🧬 Basic Research

**Mera Sun Barr, Ph.D.,** Centre for Addiction and Mental Health at the University of Toronto, Canada, will evaluate a potential biomarker of schizophrenia and of patients' response to a treatment called repetitive transcranial magnetic stimulation (rTMS). If successful, this treatment could promote abstinence from cannabis, the most commonly used illicit drug among patients with schizophrenia. Cannabis is also known to exacerbate schizophrenia symptoms in some people. Dr. Barr will use cannabis outcomes to determine the effectiveness of rTMS as a treatment and the utility of brain activity known as cortical inhibition as a biomarker.

🧬 Diagnostic Tools/Early Intervention

**Hadar Ben-Yoav, Ph.D.,** Ben-Gurion University of the Negev, Israel, is developing lab-on-a-chip technology specialized for sensing the levels of a drug called clozapine in schizophrenia patients' blood. Clozapine is an often effective antipsychotic medication, yet difficulties in managing its doses have limited its use. Much like how the finger prick test transformed diabetes management by enabling real-time glucose monitoring, the new technology would employ a nanometer-thick film to provide real-time monitoring of clozapine levels in a biosensor.

🧬 New Technologies

**Maddalena Delma Caiati, M.D., Ph.D.,** Harvard University, will explore underpinnings of schizophrenia in the brain by focusing on the role of two types of molecules that affect brain cell growth. Both brain-derived neurotrophic factor (BDNF) and neuregulins are growth factors that have been linked to schizophrenia. Using mouse models, Dr. Caiati aims to disentangle the relative contributions of the BDNF, neuregulins, and the neurotransmitter dopamine in the development of the prefrontal cortex, the brain area responsible for many aspects of cognition.

🧬 Basic Research

**Sarah E. Canetta, Ph.D.,** Columbia University, aims to illuminate ways in which relatively subtle changes in activity within the developing brain may give rise to the large-scale brain "mis-wiring" suspected to give rise to schizophrenia. Experiments in mice will test the hypothesis that a brief decrease in the level of connection between two brain areas associated with schizophrenia, the mediodorsal nucleus of the thalamus and the prefrontal cortex, is sufficient to cause permanent mis-wiring. These results will inform a study in humans that will examine whether the relative strength of the connections between these brain regions is affected in unmedicated patients with schizophrenia.

🧬 Basic Research

**Molly Erickson, Ph.D.,** Rutgers University, will test the feasibility of a new potential therapy known as neurofeedback for working memory impairments in schizophrenia patient. Deficits in working memory are a common cognitive impairment in people with schizophrenia. Dr. Erickson aims to determine whether schizophrenia patients can learn to momentarily enhance or suppress a certain type of brain activity linked to working memory capacity in response to visual or auditory cues.

🧬 Next-Generation Therapies

**Mar Fatjo-vilas, Ph.D.,** FIDMAG Research Foundation, Spain, is interested in the idea that the causes of schizophrenia include an evolutionary component that can be detected by studying the genome. Dr. Fatjo-vilas will examine sections of the genome known as human accelerated regions (HARs), characterized by significant changes that occurred after humans diverged from chimpanzees. Machine learning

algorithms may will provide insights into the role of HARs in brain structure differences observed in schizophrenia patients compared to healthy subjects.

IDOI Basic Research

**Katie Ferguson, Ph.D.,** Yale University, aims to determine whether changes in inhibitory interneurons can cause brain changes observed in schizophrenia. Inhibitory interneurons act as a "brake system" in the brain, and schizophrenia symptoms may arise when this function is disrupted. Using a technique called optogenetics, the team will stop the activity of specific groups of inhibitory interneurons in lab animals and measure the effect on other cells. This is one of several approaches that Dr. Ferguson will use to determine if changes in inhibitory interneurons can replicate brain changes seen in schizophrenia.

IDOI Basic Research

**Tom P. Franken, M.D., Ph.D.,** Salk Institute for Biological Studies, will study the process that allow the brain to make judgements in the face of uncertainty, known as probabilistic interference, which is disrupted in schizophrenia. The team will focus on the feedback connections that are thought to deliver sensory information from lower brain areas the higher brain areas that make decisions. By probing the brains of macaques, a type of primate, Dr. Franken aims to reveal how disruptions in brain circuits involved in probabilistic interference give rise to schizophrenia symptoms.

IDOI Basic Research

**Eilis Hannon, Ph.D.,** University of Exeter, U.K., will test the idea that alternative RNA splicing may contribute to schizophrenia. Alternative splicing is an editing process through which the same gene can encode a variety of different protein products. Noting that schizophrenia arises from variations at hundreds of sites within the genome, each contributing a small increase to an individual's genetic risk, Dr. Hannon aims to identify genes whose products are found in different forms in the brains of schizophrenia patients compared to healthy people.

IDOI Basic Research

**Sami Hassan, Ph.D.,** Columbia University, will analyze the networks within a brain region called CA2 in an effort to determine whether it may provide a new target for schizophrenia treatment. Previous evidence suggests that CA2 is critical for social memory formation, which is known to be disrupted in schizophrenia. Dr. Hassan aims to gain new insights into this region and its role in social learning by imaging the brain in mice as they perform a social memory task.

IDOI Basic Research

**Colin Shaun Hawco, Ph.D.,** Centre for Addiction and Mental Health, University of Toronto, Canada, will search for clusters of schizophrenia patients with deficits in specific brain circuits thought to drive patterns of social-cognitive deficits. Using data from brain imaging and a battery of social-cognitive tests, the team will identify groups of with similar combinations of features among a large sample of patients and healthy people. By linking deficits in social cognitive performance with distinct biological changes, Dr. Hawco hopes to find specific brain circuit disruptions involved in the social deficits characteristic of schizophrenia.

IDOI Basic Research

**Gabriel E. Hoffman, Ph.D.,** Icahn School of Medicine at Mount Sinai, will use a computational approach to analyze large-scale epigenomic phenomena (chemical modifications of DNA) that may be related to the molecular mechanisms behind schizophrenia. The data analyzed comes from the PsychENCODE Consortium, a massive public repository of brain-related genomic data. Dr. Hoffman will look for genetic alterations that may increase the risk of schizophrenia by modifying gene regulation in a specific cell type, region of the brain, or developmental time point to disrupt normal brain function.

IDOI Basic Research

**Liang-Tien Hsieh, Ph.D.,** University of California, Davis Medical Center, will use a variety of imaging techniques, including EEG and fMRI, to learn more about the neural basis underlying memory deficits in people with schizophrenia. Both short-term and long-term memory can be disrupted in schizophrenia, and new evidence suggests that the dis

order may impair a person's ability to remember events in temporal order while leaving their memories of individual items or events intact. The study will search for the specific neural circuitry that contributes to these selective problems with memory.

IIIDCIII Basic Research

**Simona Keller, Ph.D.,** University of Naples Federico II, Italy, will investigate the full landscape of gene alterations that affect D-amino acids, which have been identified as possible contributors to the start and progression of schizophrenia. Although researchers know about some of the enzymes that regulate their creation and destruction, Dr. Keller hopes to learn more about how the genes encoding these enzymes are modified. Her hypothesis is that a particular type of gene modification called DNA methylation may be necessary for correct brain development, and that methylation anomalies may lead to changes in gene expression that result in D-amino acid dysregulation, affecting schizophrenia risk.

IIIDCIII Basic Research

**Jerillyn S. Kent, Ph.D.,** University of Minnesota, hopes to learn more about how abnormal motor function in some people with schizophrenia may influence their social cognition. Dr. Kent will be focusing on motor resonance, which refers to brain activity occurring when a person performs an action or watches another person perform it. She will be testing a hypothesis that motor impairments such as head jerking in patients may be related to motor resonance impairments, as well as examining how motor resonance impairments are related to overall social cognition difficulties.

IIIDCIII Basic Research

**Takashi Kitamura, Ph.D.,** University of Texas Southwestern Medical Center at Dallas, hopes to learn more about the neural circuits that underlie auditory and visual hallucinations in people with schizophrenia. Previous research has demonstrated that the brain's entorhinal-hippocampal neural network may help the brain to filter out unnecessary information that causes these forms of psychosis, but details of this network's functioning are unclear. Dr. Kitamura has discovered a new cell population in this region, called island

cells, which may be dysfunctional in schizophrenia patients. He will examine how island cells behave normally and how they may be impaired or inactivated in laboratory cell cultures and in animal models of schizophrenia.

IIIDCIII Basic Research

**Ellen Eun-Ok Lee, M.D.,** University of California, San Diego, plans to study the role in people with schizophrenia of adiponectin, a metabolic hormone secreted by fat cells, in aging, metabolic function, cognition and depression. Patients often have increased insulin resistance and inflammation that can lead to diabetes and obesity and premature death. Dr. Lee will compare adiponectin levels and physical and mental health assessments between people with schizophrenia and controls, to gather data that may eventually guide interventions that target adiponectin levels in people with schizophrenia.

IIIDCIII Basic Research

**Leslie Giselle Nucifora, Ph.D.,** Johns Hopkins University, will build on preliminary research showing that a subset of patients with schizophrenia have increased protein insolubility. Changes in cellular stress and inflammation, which have been reported in some patients, may also lead to insolubility. The goal is to study postmortem brains from patients to determine whether protein insolubility affects a specific region in these brains (olfactory neurons are a suspected target) and to determine what kinds of neurocognitive deficits may arise from protein insolubility.

IIIDCIII Basic Research

**Shauna Lee Parkes, Ph.D.,** Universite Bordeaux II, France, hopes to learn more about the neural pathways in the brain that help people perform "goal-directed" behaviors—making decisions to take actions that will lead to valuable outcomes. People with schizophrenia often have poor goal-directed control, but the reasons are unclear. The study will examine the communication pathways in humans and mice between the brain's cortex and hippocampus, to determine whether this circuitry is involved in goal-directed control. Dr. Parkes will focus especially on the role of these circuits in providing context for decision-making—another deficit seen in schizophrenia--so that a person's behavior aligns with his or her goals.

IIIDCIII Basic Research

**Quentin Perrenoud, Ph.D.,** Yale University, will be studying the development of peri-neuronal nets (PNNs) in the brain, and how their maturation may impact the onset of schizophrenia. Symptoms develop during early adulthood when PNNs appear in the cerebral cortex. PNNs are altered in schizophrenia patients, and genes involved in PNN metabolism have been linked to the disease. The research seeks to determine how PNNs alter the activity of the mouse cortex, to confirm whether a protein called ErbB4 is essential to the maturation of PNNs, and to observe how PNNs and ErbB4 impact a learning task in the mice.

▶ Basic Research

**Benjamin C. Reiner, Ph.D.,** University of Pennsylvania, will investigate the genetic basis of schizophrenia by looking at the DNA in individual brain cells. Previous research has found that among people with schizophrenia, neurons show more "jumping DNA," or elements that randomly move to different locations in the genome. The study will use brain samples from patients to identify the number and location of these "jumping" elements, to better understand genetic variations that can give rise to—and be targeted to treat—schizophrenia.

▶ Basic Research

**Christin Schifani, Ph.D.,** Centre of Addiction and Mental Health, University of Toronto, Canada, will test the theory that schizophrenia results from developmental disruptions to the brain. Prior research has linked schizophrenia to excessive pruning, in which the developing brain removes superfluous connections between cells. Dr. Schifani will use positron emission tomography in patients to investigate whether schizophrenia symptoms correspond with abnormally few connections in the brain, and with any difference in brain volume. He hopes the findings will make it easier to identify schizophrenia while it develops in late adolescence and early adulthood.

▶ Diagnostic tools/early intervention

**Joseph James Shaffer, Ph.D.,** University of Iowa, seeks to pinpoint and treat the brain regions that underlie cognitive symptoms in schizophrenia. His team will look at activity in two implicated brain regions: the cerebellum, which coordinates muscle activity, and medial prefrontal cortex, which directs higher-level processing. They expect to find that people with schizophrenia show abnormally low activity in both regions, as measured by functional magnetic resonance imaging. They will also test whether applying transcranial magnetic stimulation to the cerebellum restores activity in medial prefrontal cortex to normal levels, pointing toward TMS as a potential treatment for cognitive symptoms.

▶ Next-Generation Therapies

**Ping Su, Ph.D.,** Centre for Addiction and Mental Health, University of Toronto, Canada, will evaluate a potential new treatment for schizophrenia. Previously Dr. Su identified a short protein called TAT-D2pep that successfully reverses symptoms of schizophrenia in animal models without the side effects normally associated with antipsychotic drugs. Now, Dr. Su will investigate the safety, dosage, efficacy, and administration method for the drug before seeking to introduce it to patients in clinic trials.

▶ Next-Generation Therapies

**Halene Tobias, M.D., Ph.D.,** Icahn School of Medicine at Mount Sinai, will look for new genetic targets that may represent potential treatment options for schizophrenia. The work will focus on specific cell types to identify changes in gene expression in patients. For Dr. Tobias, this represents the first step in developing a pipeline to identify novel genetic treatment approaches for the illness.

▶ Basic Research

**John B. Torous, M.D.,** Beth Israel Deaconess Medical Center, Harvard University, will look for markers that will help predict which patients with schizophrenia will relapse. The study takes advantage of smartphone technology and wearable sensors that will allow researchers to track symptoms, including heart rate and sleep disruptance, to identify markers that are associated with relapse. Dr. Torous will use this information to better understand the factors that contribute to relapse in schizophrenia.

▶ Diagnostic Tools/Early Intervention

**Jari G. Willing, Ph.D.,** University of Illinois at Urbana-Champaign, will explore the role of environmental factors, like endocrine disruptors and maternal infections in the development of schizophrenia later in life. The work will use a rat model to determine if the combination of chemical exposure and maternal infection in utero increases schizophrenia symptoms. Dr. Willing's work may elucidate a novel environmental mechanism for the development of schizophrenia that could be therapeutically addressed via prompt treatment or prevention of maternal infection.

Basic Research

# SUICIDE PREVENTION

**Henry William Chase, Ph.D.,** University of Pittsburgh, will study transcranial direct current stimulation (tDCS), a promising new treatment for mood disorders, in the context of suicidal ideation and behavior. The study will focus on a brain region known as the left ventrolateral prefrontal cortex, the activity of which has been linked to impulsivity-related symptoms such as those involved in suicide. Dr. Chase wills apply tDCS to this brain region in an effort to regulate its function.

Next-Generation Therapies

**Sakina Rizvi, Ph.D.,** University of Toronto, Canada, will probe a brain network linked to suicide risk and study how that network is affected by opioids--a potential preventive treatment. People are more likely to harm themselves when they believe they can tolerate high levels of pain, an experience that opioids reduce. Dr. Rizvik will use functional magnetic resonance imaging to identify how the relevant brain networks respond to opioids among people with depression, who have increased suicide risk. The results could shed light on the biology of suicide risk, which is typically difficult to predict.

Basic Research

# OTHER DISORDERS
*Rett Syndrome*

**Annie Vogel Ciernia, Ph.D.,** University of California, Davis, will explore the molecular underpinnings of Rett syndrome. The spontaneous disorder, which shares many symptoms with autism spectrum disorders, is caused by defects in a gene known as MeCP2. Dr. Vogel Ciernia will study two different variants of MeCP2 to determine how they contribute to the development of Rett syndrome.

Basic Research

**Ralf S. Schmid, Ph.D.,** University of North Carolina at Chapel Hill, will test a potential treatment for Rett Syndrome, a serious neurodevelopmental disorder that affects 1 in 10,000 girls. The disorder is caused by a mutation to the gene MeCP2, whereby functioning copies of the gene are sometimes inactivated. Dr. Schmid will attempt a gene editing technique to reactivate healthy copies of MeCP2 without changing the genetic code itself. He hopes to then test this technique in mouse models of Rett Syndrome.

Next-Generation Therapies

# The Following Institutions Had Three or More Young Investigator Grantees This Year:

| UNIVERSITY | GRANTEES |
|---|---|
| Icahn School of Medicine at Mount Sinai | 8 |
| University of California (System) | 8 |
| University of Pittsburgh | 8 |
| New York University | 7 |
| University of Toronto, Canada | 7 |
| Yale University | 7 |
| Columbia University | 6 |
| Johns Hopkins University | 6 |
| Cornell University / Weill Cornell Medical College | 5 |
| National Institute of Mental Health (NIMH/NIH) | 5 |
| University of North Carolina at Chapel Hill | 5 |
| University of Texas (System) | 5 |
| Harvard University / Harvard Medical School | 4 |
| Massachusetts General Hospital | 4 |
| Cold Spring Harbor Laboratory | 3 |
| Massachusetts Institute of Technology | 3 |
| Max Planck Institute, Germany | 3 |
| Northwestern University | 3 |
| Rutgers University | 3 |
| Stanford University | 3 |
| State University of New York (SUNY System) | 3 |

## AWARDED TO SCIENTISTS

# $380 MILLION

## GRANTS

# 5,500

**The breakdown of our grantees since 1987**

4,282 **Young Investigators**
828 **Independent Investigators**
409 **Distinguished Investigators**

## UNIVERSITIES & MEDICAL CENTERS

# 550

## COUNTRIES, INCLUDING THE U.S.

# 35

## 177 ACTIVE SCIENTIFIC COUNCIL MEMBERS (AND 7 EMERITUS MEMBERS)

The **all-volunteer** Foundation Scientific Council **is composed of leading experts across disciplines in brain & behavior research who review grant applications and recommend the most promising ideas to fund.**

**The group includes:**

52 **Members of the National Academy of Medicine**
26 **Chairs of Psychiatry & Neuroscience Departments**
13 **Members of the National Academy of Sciences**
4 **Recipients of the National Medal of Science**
2 **Former Directors of the National Institute of Mental Health and the Current Director**
2 **Nobel Prize Winners**

# Investing in Breakthroughs to Find a Cure

100% of donor contributions for research are invested in our grants leading to advances and breakthroughs in brain and behavior research. This is made possible by the generous support of two family foundations which cover the Foundation's operating expenses.

## OUR MISSION:
The Brain & Behavior Research Foundation is committed to alleviating the suffering caused by mental illness by awarding grants that will lead to advances and breakthroughs in scientific research.

## HOW WE DO IT:
The Foundation funds the most innovative ideas in neuroscience and psychiatry to better understand the causes and develop new ways to treat brain and behavior disorders. These disorders include depression, bipolar disorder, schizophrenia, autism, attention-deficit hyperactivity disorder, anxiety, borderline personality disorder, chemical dependency, obsessive-compulsive disorder and post-traumatic stress disorders.

## OUR CREDENTIALS:
Since 1987 the Foundation has awarded $380 million to fund more than 5,500 grants to more than 4,500 leading scientists around the world. This has led to over $3.8 billion in additional funding for these scientists.

## OUR VISION:
To dramatically improve the lives of those with mental illness and ultimately enable people to live full, happy and productive lives.